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(54) Title: COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER			
(57) Abstract			
<p>Compounds and methods for the treatment and diagnosis of lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or DNA molecules encoding such polypeptides, are also provided, together with DNA molecules for preparing the inventive polypeptides.</p>			

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## COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER

### TECHNICAL FIELD

5           The present invention relates generally to therapy and diagnosis of cancer, such as lung cancer. The invention is more specifically related to polypeptides comprising at least a portion of a lung tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of lung cancer, and for the  
10       diagnosis and monitoring of such cancers.

### BACKGROUND OF THE INVENTION

          Lung cancer is the primary cause of cancer death among both men and women in the U.S., with an estimated 172,000 new cases being reported in 1994. The five-year survival rate among all lung cancer patients, regardless of the stage of disease  
15       at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among cases detected while the disease is still localized. However, only 16% of lung cancers are discovered before the disease has spread.

          Early detection is difficult since clinical symptoms are often not seen until the disease has reached an advanced stage. Currently, diagnosis is aided by the  
20       use of chest x-rays, analysis of the type of cells contained in sputum and fiberoptic examination of the bronchial passages. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. In spite of considerable research into therapies for the disease, lung cancer remains difficult to treat.

25           Accordingly, there remains a need in the art for improved vaccines, treatment methods and diagnostic techniques for lung cancer.

### SUMMARY OF THE INVENTION

          Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as lung cancer. In one aspect, the present

invention provides polypeptides comprising at least a portion of a lung tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347 and 349; (b) variants of a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347 and 349; and (c) complements of a sequence of (a) or (b). In specific embodiments, the polypeptides of the present invention comprise at least a portion of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 152, 155, 156, 165, 166, 169, 170, 172, 174, 176, 226-252, 338-344 and 346, and variants thereof.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a lung tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.



The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a lung tumor protein; and (b) a physiologically acceptable carrier.

5        Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

10        Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above, and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

15        Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

20        Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a lung tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

25        Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

30

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a lung tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Determined T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells determined from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a lung tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be lung cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the

sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

5

#### SEQUENCE IDENTIFIERS

- SEQ ID NO: 1 is the determined cDNA sequence for LST-S1-2  
SEQ ID NO: 2 is the determined cDNA sequence for LST-S1-28  
SEQ ID NO: 3 is the determined cDNA sequence for LST-S1-90  
10 SEQ ID NO: 4 is the determined cDNA sequence for LST-S1-144  
SEQ ID NO: 5 is the determined cDNA sequence for LST-S1-133  
SEQ ID NO: 6 is the determined cDNA sequence for LST-S1-169  
SEQ ID NO: 7 is the determined cDNA sequence for LST-S2-6  
SEQ ID NO: 8 is the determined cDNA sequence for LST-S2-11  
15 SEQ ID NO: 9 is the determined cDNA sequence for LST-S2-17  
SEQ ID NO: 10 is the determined cDNA sequence for LST-S2-25  
SEQ ID NO: 11 is the determined cDNA sequence for LST-S2-39  
SEQ ID NO: 12 is a first determined cDNA sequence for LST-S2-43  
SEQ ID NO: 13 is a second determined cDNA sequence for LST-S2-43  
20 SEQ ID NO: 14 is the determined cDNA sequence for LST-S2-65  
SEQ ID NO: 15 is the determined cDNA sequence for LST-S2-68  
SEQ ID NO: 16 is the determined cDNA sequence for LST-S2-72  
SEQ ID NO: 17 is the determined cDNA sequence for LST-S2-74  
SEQ ID NO: 18 is the determined cDNA sequence for LST-S2-103  
25 SEQ ID NO: 19 is the determined cDNA sequence for LST-S2-N1-1F  
SEQ ID NO: 20 is the determined cDNA sequence for LST-S2-N1-2A  
SEQ ID NO: 21 is the determined cDNA sequence for LST-S2-N1-4H  
SEQ ID NO: 22 is the determined cDNA sequence for LST-S2-N1-5A  
SEQ ID NO: 23 is the determined cDNA sequence for LST-S2-N1-6B  
30 SEQ ID NO: 24 is the determined cDNA sequence for LST-S2-N1-7B  
SEQ ID NO: 25 is the determined cDNA sequence for LST-S2-N1-7H

- SEQ ID NO: 26 is the determined cDNA sequence for LST-S2-N1-8A  
SEQ ID NO: 27 is the determined cDNA sequence for LST-S2-N1-8D  
SEQ ID NO: 28 is the determined cDNA sequence for LST-S2-N1-9A  
SEQ ID NO: 29 is the determined cDNA sequence for LST-S2-N1-9E  
5 SEQ ID NO: 30 is the determined cDNA sequence for LST-S2-N1-10A  
SEQ ID NO: 31 is the determined cDNA sequence for LST-S2-N1-10G  
SEQ ID NO: 32 is the determined cDNA sequence for LST-S2-N1-11A  
SEQ ID NO: 33 is the determined cDNA sequence for LST-S2-N1-12C  
SEQ ID NO: 34 is the determined cDNA sequence for LST-S2-N1-12E  
10 SEQ ID NO: 35 is the determined cDNA sequence for LST-S2-B1-3D  
SEQ ID NO: 36 is the determined cDNA sequence for LST-S2-B1-6C  
SEQ ID NO: 37 is the determined cDNA sequence for LST-S2-B1-5D  
SEQ ID NO: 38 is the determined cDNA sequence for LST-S2-B1-5F  
SEQ ID NO: 39 is the determined cDNA sequence for LST-S2-B1-6G  
15 SEQ ID NO: 40 is the determined cDNA sequence for LST-S2-B1-8A  
SEQ ID NO: 41 is the determined cDNA sequence for LST-S2-B1-8D  
SEQ ID NO: 42 is the determined cDNA sequence for LST-S2-B1-10A  
SEQ ID NO: 43 is the determined cDNA sequence for LST-S2-B1-9B  
SEQ ID NO: 44 is the determined cDNA sequence for LST-S2-B1-9F  
20 SEQ ID NO: 45 is the determined cDNA sequence for LST-S2-B1-12D  
SEQ ID NO: 46 is the determined cDNA sequence for LST-S2-I2-2B  
SEQ ID NO: 47 is the determined cDNA sequence for LST-S2-I2-5F  
SEQ ID NO: 48 is the determined cDNA sequence for LST-S2-I2-6B  
SEQ ID NO: 49 is the determined cDNA sequence for LST-S2-I2-7F  
25 SEQ ID NO: 50 is the determined cDNA sequence for LST-S2-I2-8G  
SEQ ID NO: 51 is the determined cDNA sequence for LST-S2-I2-9E  
SEQ ID NO: 52 is the determined cDNA sequence for LST-S2-I2-12B  
SEQ ID NO: 53 is the determined cDNA sequence for LST-S2-H2-2C  
SEQ ID NO: 54 is the determined cDNA sequence for LST-S2-H2-1G  
30 SEQ ID NO: 55 is the determined cDNA sequence for LST-S2-H2-4G  
SEQ ID NO: 56 is the determined cDNA sequence for LST-S2-H2-3H

- SEQ ID NO: 57 is the determined cDNA sequence for LST-S2-H2-5G  
SEQ ID NO: 58 is the determined cDNA sequence for LST-S2-H2-9B  
SEQ ID NO: 59 is the determined cDNA sequence for LST-S2-H2-10H  
SEQ ID NO: 60 is the determined cDNA sequence for LST-S2-H2-12D  
5 SEQ ID NO: 61 is the determined cDNA sequence for LST-S3-2  
SEQ ID NO: 62 is the determined cDNA sequence for LST-S3-4  
SEQ ID NO: 63 is the determined cDNA sequence for LST-S3-7  
SEQ ID NO: 64 is the determined cDNA sequence for LST-S3-8  
SEQ ID NO: 65 is the determined cDNA sequence for LST-S3-12  
10 SEQ ID NO: 66 is the determined cDNA sequence for LST-S3-13  
SEQ ID NO: 67 is the determined cDNA sequence for LST-S3-14  
SEQ ID NO: 68 is the determined cDNA sequence for LST-S3-16  
SEQ ID NO: 69 is the determined cDNA sequence for LST-S3-21  
SEQ ID NO: 70 is the determined cDNA sequence for LST-S3-22  
15 SEQ ID NO: 71 is the determined cDNA sequence for LST-S1-7  
SEQ ID NO: 72 is the determined cDNA sequence for LST-S1-A-1E  
SEQ ID NO: 73 is the determined cDNA sequence for LST-S1-A-1G  
SEQ ID NO: 74 is the determined cDNA sequence for LST-S1-A-3E  
SEQ ID NO: 75 is the determined cDNA sequence for LST-S1-A-4E  
20 SEQ ID NO: 76 is the determined cDNA sequence for LST-S1-A-6D  
SEQ ID NO: 77 is the determined cDNA sequence for LST-S1-A-8D  
SEQ ID NO: 78 is the determined cDNA sequence for LST-S1-A-10A  
SEQ ID NO: 79 is the determined cDNA sequence for LST-S1-A-10C  
SEQ ID NO: 80 is the determined cDNA sequence for LST-S1-A-9D  
25 SEQ ID NO: 81 is the determined cDNA sequence for LST-S1-A-10D  
SEQ ID NO: 82 is the determined cDNA sequence for LST-S1-A-9H  
SEQ ID NO: 83 is the determined cDNA sequence for LST-S1-A-11D  
SEQ ID NO: 84 is the determined cDNA sequence for LST-S1-A-12D  
SEQ ID NO: 85 is the determined cDNA sequence for LST-S1-A-11E  
30 SEQ ID NO: 86 is the determined cDNA sequence for LST-S1-A-12E  
SEQ ID NO: 87 is the determined cDNA sequence for L513S (T3).

- SEQ ID NO: 88 is the determined cDNA sequence for L513S contig 1.
- SEQ ID NO: 89 is a first determined cDNA sequence for L514S.
- SEQ ID NO: 90 is a second determined cDNA sequence for L514S.
- SEQ ID NO: 91 is a first determined cDNA sequence for L516S.
- 5 SEQ ID NO: 92 is a second determined cDNA sequence for L516S.
- SEQ ID NO: 93 is the determined cDNA sequence for L517S.
- SEQ ID NO: 94 is the extended cDNA sequence for LST-S1-169 (also known as L519S).
- SEQ ID NO: 95 is a first determined cDNA sequence for L520S.
- 10 SEQ ID NO: 96 is a second determined cDNA sequence for L520S.
- SEQ ID NO: 97 is a first determined cDNA sequence for L521S.
- SEQ ID NO: 98 is a second determined cDNA sequence for L521S.
- SEQ ID NO: 99 is the determined cDNA sequence for L522S.
- SEQ ID NO: 100 is the determined cDNA sequence for L523S.
- 15 SEQ ID NO: 101 is the determined cDNA sequence for L524S.
- SEQ ID NO: 102 is the determined cDNA sequence for L525S.
- SEQ ID NO: 103 is the determined cDNA sequence for L526S.
- SEQ ID NO: 104 is the determined cDNA sequence for L527S.
- SEQ ID NO: 105 is the determined cDNA sequence for L528S.
- 20 SEQ ID NO: 106 is the determined cDNA sequence for L529S.
- SEQ ID NO: 107 is a first determined cDNA sequence for L530S.
- SEQ ID NO: 108 is a second determined cDNA sequence for L530S.
- SEQ ID NO: 109 is the determined full-length cDNA sequence for L531S short form
- SEQ ID NO: 110 is the predicted amino acid sequence encoded by SEQ ID NO: 109.
- 25 SEQ ID NO: 111 is the determined full-length cDNA sequence for L531S long form
- SEQ ID NO: 112 is the predicted amino acid sequence encoded by SEQ ID NO: 111.
- SEQ ID NO: 113 is the determined full-length cDNA sequence for L520S.
- SEQ ID NO: 114 is the predicted amino acid sequence encoded by SEQ ID NO: 113.
- SEQ ID NO: 115 is the determined cDNA sequence for contig 1.
- 30 SEQ ID NO: 116 is the determined cDNA sequence for contig 3.
- SEQ ID NO: 117 is the determined cDNA sequence for contig 4.

- SEQ ID NO: 118 is the determined cDNA sequence for contig 5.  
SEQ ID NO: 119 is the determined cDNA sequence for contig 7.  
SEQ ID NO: 120 is the determined cDNA sequence for contig 8.  
SEQ ID NO: 121 is the determined cDNA sequence for contig 9.  
5 SEQ ID NO: 122 is the determined cDNA sequence for contig 10.  
SEQ ID NO: 123 is the determined cDNA sequence for contig 12.  
SEQ ID NO: 124 is the determined cDNA sequence for contig 11.  
SEQ ID NO: 125 is the determined cDNA sequence for contig 13.  
SEQ ID NO: 126 is the determined cDNA sequence for contig 15.  
10 SEQ ID NO: 127 is the determined cDNA sequence for contig 16.  
SEQ ID NO: 128 is the determined cDNA sequence for contig 17.  
SEQ ID NO: 129 is the determined cDNA sequence for contig 19.  
SEQ ID NO: 130 is the determined cDNA sequence for contig 20.  
SEQ ID NO: 131 is the determined cDNA sequence for contig 22.  
15 SEQ ID NO: 132 is the determined cDNA sequence for contig 24.  
SEQ ID NO: 133 is the determined cDNA sequence for contig 29.  
SEQ ID NO: 134 is the determined cDNA sequence for contig 31.  
SEQ ID NO: 135 is the determined cDNA sequence for contig 33.  
SEQ ID NO: 136 is the determined cDNA sequence for contig 38.  
20 SEQ ID NO: 137 is the determined cDNA sequence for contig 39.  
SEQ ID NO: 138 is the determined cDNA sequence for contig 41.  
SEQ ID NO: 139 is the determined cDNA sequence for contig 43.  
SEQ ID NO: 140 is the determined cDNA sequence for contig 44.  
SEQ ID NO: 141 is the determined cDNA sequence for contig 45.  
25 SEQ ID NO: 142 is the determined cDNA sequence for contig 47.  
SEQ ID NO: 143 is the determined cDNA sequence for contig 48.  
SEQ ID NO: 144 is the determined cDNA sequence for contig 49.  
SEQ ID NO: 145 is the determined cDNA sequence for contig 50.  
SEQ ID NO: 146 is the determined cDNA sequence for contig 53.  
30 SEQ ID NO: 147 is the determined cDNA sequence for contig 54.  
SEQ ID NO: 148 is the determined cDNA sequence for contig 56.



- SEQ ID NO: 149 is the determined cDNA sequence for contig 57.
- SEQ ID NO: 150 is the determined cDNA sequence for contig 58.
- SEQ ID NO: 151 is the full-length cDNA sequence for L530S.
- SEQ ID NO: 152 is the amino acid sequence encoded by SEQ ID NO: 151
- 5 SEQ ID NO: 153 is the full-length cDNA sequence of a first variant of L514S
- SEQ ID NO: 154 is the full-length cDNA sequence of a second variant of L514S
- SEQ ID NO: 155 is the amino acid sequence encoded by SEQ ID NO: 153.
- SEQ ID NO: 156 is the amino acid sequence encoded by SEQ ID NO: 154.
- SEQ ID NO: 157 is the determined cDNA sequence for contig 59.
- 10 SEQ ID NO: 158 is the full-length cDNA sequence for L763P (also referred to as contig 22).
- SEQ ID NO: 159 is the amino acid sequence encoded by SEQ ID NO: 158.
- SEQ ID NO: 160 is the full-length cDNA sequence for L762P (also referred to as contig 17).
- 15 SEQ ID NO: 161 is the amino acid sequence encoded by SEQ ID NO: 160.
- SEQ ID NO: 162 is the determined cDNA sequence for L515S.
- SEQ ID NO: 163 is the full-length cDNA sequence of a first variant of L524S.
- SEQ ID NO: 164 is the full-length cDNA sequence of a second variant of L524S.
- SEQ ID NO: 165 is the amino acid sequence encoded by SEQ ID NO: 163.
- 20 SEQ ID NO: 166 is the amino acid sequence encoded by SEQ ID NO: 164.
- SEQ ID NO: 167 is the full-length cDNA sequence of a first variant of L762P.
- SEQ ID NO: 168 is the full-length cDNA sequence of a second variant of L762P.
- SEQ ID NO: 169 is the amino acid sequence encoded by SEQ ID NO: 167.
- SEQ ID NO: 170 is the amino acid sequence encoded by SEQ ID NO: 168.
- 25 SEQ ID NO: 171 is the full-length cDNA sequence for L773P (also referred to as contig 56).
- SEQ ID NO: 172 is the amino acid sequence encoded by SEQ ID NO: 171.
- SEQ ID NO: 173 is an extended cDNA sequence for L519S.
- SEQ ID NO: 174 is the predicted amino acid sequence encoded by SEQ ID NO: 174.
- 30 SEQ ID NO: 175 is the full-length cDNA sequence for L523S.
- SEQ ID NO: 176 is the predicted amino acid sequence encoded by SEQ ID NO: 175.

- SEQ ID NO: 177 is the determined cDNA sequence for LST-sub5-7A.  
SEQ ID NO: 178 is the determined cDNA sequence for LST-sub5-8G.  
SEQ ID NO: 179 is the determined cDNA sequence for LST-sub5-8H.  
SEQ ID NO: 180 is the determined cDNA sequence for LST-sub5-10B.  
5 SEQ ID NO: 181 is the determined cDNA sequence for LST-sub5-10H.  
SEQ ID NO: 182 is the determined cDNA sequence for LST-sub5-12B.  
SEQ ID NO: 183 is the determined cDNA sequence for LST-sub5-11C.  
SEQ ID NO: 184 is the determined cDNA sequence for LST-sub6-1c.  
SEQ ID NO: 185 is the determined cDNA sequence for LST-sub6-2f.  
10 SEQ ID NO: 186 is the determined cDNA sequence for LST-sub6-2G.  
SEQ ID NO: 187 is the determined cDNA sequence for LST-sub6-4d.  
SEQ ID NO: 188 is the determined cDNA sequence for LST-sub6-4e.  
SEQ ID NO: 189 is the determined cDNA sequence for LST-sub6-4f.  
SEQ ID NO: 190 is the determined cDNA sequence for LST-sub6-3h.  
15 SEQ ID NO: 191 is the determined cDNA sequence for LST-sub6-5d.  
SEQ ID NO: 192 is the determined cDNA sequence for LST-sub6-5h.  
SEQ ID NO: 193 is the determined cDNA sequence for LST-sub6-6h.  
SEQ ID NO: 194 is the determined cDNA sequence for LST-sub6-7a.  
SEQ ID NO: 195 is the determined cDNA sequence for LST-sub6-8a.  
20 SEQ ID NO: 196 is the determined cDNA sequence for LST-sub6-7d.  
SEQ ID NO: 197 is the determined cDNA sequence for LST-sub6-7e.  
SEQ ID NO: 198 is the determined cDNA sequence for LST-sub6-8e.  
SEQ ID NO: 199 is the determined cDNA sequence for LST-sub6-7g.  
SEQ ID NO: 200 is the determined cDNA sequence for LST-sub6-9f.  
25 SEQ ID NO: 201 is the determined cDNA sequence for LST-sub6-9h.  
SEQ ID NO: 202 is the determined cDNA sequence for LST-sub6-11b.  
SEQ ID NO: 203 is the determined cDNA sequence for LST-sub6-11c.  
SEQ ID NO: 204 is the determined cDNA sequence for LST-sub6-12c.  
SEQ ID NO: 205 is the determined cDNA sequence for LST-sub6-12e.  
30 SEQ ID NO: 206 is the determined cDNA sequence for LST-sub6-12f.  
SEQ ID NO: 207 is the determined cDNA sequence for LST-sub6-11g.

- SEQ ID NO: 208 is the determined cDNA sequence for LST-sub6-12g.  
SEQ ID NO: 209 is the determined cDNA sequence for LST-sub6-12h.  
SEQ ID NO: 210 is the determined cDNA sequence for LST-sub6-II-1a.  
SEQ ID NO: 211 is the determined cDNA sequence for LST-sub6-II-2b.  
5 SEQ ID NO: 212 is the determined cDNA sequence for LST-sub6-II-2g.  
SEQ ID NO: 213 is the determined cDNA sequence for LST-sub6-II-1h.  
SEQ ID NO: 214 is the determined cDNA sequence for LST-sub6-II-4a.  
SEQ ID NO: 215 is the determined cDNA sequence for LST-sub6-II-4b.  
SEQ ID NO: 216 is the determined cDNA sequence for LST-sub6-II-3e.  
10 SEQ ID NO: 217 is the determined cDNA sequence for LST-sub6-II-4f.  
SEQ ID NO: 218 is the determined cDNA sequence for LST-sub6-II-4g.  
SEQ ID NO: 219 is the determined cDNA sequence for LST-sub6-II-4h.  
SEQ ID NO: 220 is the determined cDNA sequence for LST-sub6-II-5c.  
SEQ ID NO: 221 is the determined cDNA sequence for LST-sub6-II-5e.  
15 SEQ ID NO: 222 is the determined cDNA sequence for LST-sub6-II-6f.  
SEQ ID NO: 223 is the determined cDNA sequence for LST-sub6-II-5g.  
SEQ ID NO: 224 is the determined cDNA sequence for LST-sub6-II-6g.  
SEQ ID NO: 225 is the amino acid sequence for L528S.  
SEQ ID NO: 226-251 are synthetic peptides derived from L762P.  
20 SEQ ID NO: 252 is the expressed amino acid sequence of L514S.  
SEQ ID NO: 253 is the DNA sequence corresponding to SEQ ID NO: 252.  
SEQ ID NO: 254 is the DNA sequence of a L762P expression construct.  
SEQ ID NO: 255 is the determined cDNA sequence for clone 23785.  
SEQ ID NO: 256 is the determined cDNA sequence for clone 23786.  
25 SEQ ID NO: 257 is the determined cDNA sequence for clone 23788.  
SEQ ID NO: 258 is the determined cDNA sequence for clone 23790.  
SEQ ID NO: 259 is the determined cDNA sequence for clone 23793.  
SEQ ID NO: 260 is the determined cDNA sequence for clone 23794.  
SEQ ID NO: 261 is the determined cDNA sequence for clone 23795.  
30 SEQ ID NO: 262 is the determined cDNA sequence for clone 23796.  
SEQ ID NO: 263 is the determined cDNA sequence for clone 23797.

- SEQ ID NO: 264 is the determined cDNA sequence for clone 23798.
- SEQ ID NO: 265 is the determined cDNA sequence for clone 23799.
- SEQ ID NO: 266 is the determined cDNA sequence for clone 23800.
- SEQ ID NO: 267 is the determined cDNA sequence for clone 23802.
- 5 SEQ ID NO: 268 is the determined cDNA sequence for clone 23803.
- SEQ ID NO: 269 is the determined cDNA sequence for clone 23804.
- SEQ ID NO: 270 is the determined cDNA sequence for clone 23805.
- SEQ ID NO: 271 is the determined cDNA sequence for clone 23806.
- SEQ ID NO: 272 is the determined cDNA sequence for clone 23807.
- 10 SEQ ID NO: 273 is the determined cDNA sequence for clone 23808.
- SEQ ID NO: 274 is the determined cDNA sequence for clone 23809.
- SEQ ID NO: 275 is the determined cDNA sequence for clone 23810.
- SEQ ID NO: 276 is the determined cDNA sequence for clone 23811.
- SEQ ID NO: 277 is the determined cDNA sequence for clone 23812.
- 15 SEQ ID NO: 278 is the determined cDNA sequence for clone 23813.
- SEQ ID NO: 279 is the determined cDNA sequence for clone 23815.
- SEQ ID NO: 280 is the determined cDNA sequence for clone 25298.
- SEQ ID NO: 281 is the determined cDNA sequence for clone 25299.
- SEQ ID NO: 282 is the determined cDNA sequence for clone 25300.
- 20 SEQ ID NO: 283 is the determined cDNA sequence for clone 25301.
- SEQ ID NO: 284 is the determined cDNA sequence for clone 25304.
- SEQ ID NO: 285 is the determined cDNA sequence for clone 25309.
- SEQ ID NO: 286 is the determined cDNA sequence for clone 25312.
- SEQ ID NO: 287 is the determined cDNA sequence for clone 25317.
- 25 SEQ ID NO: 288 is the determined cDNA sequence for clone 25321.
- SEQ ID NO: 289 is the determined cDNA sequence for clone 25323.
- SEQ ID NO: 290 is the determined cDNA sequence for clone 25327.
- SEQ ID NO: 291 is the determined cDNA sequence for clone 25328.
- SEQ ID NO: 292 is the determined cDNA sequence for clone 25332.
- 30 SEQ ID NO: 293 is the determined cDNA sequence for clone 25333.
- SEQ ID NO: 294 is the determined cDNA sequence for clone 25336.

- SEQ ID NO: 295 is the determined cDNA sequence for clone 25340.  
SEQ ID NO: 296 is the determined cDNA sequence for clone 25342.  
SEQ ID NO: 297 is the determined cDNA sequence for clone 25356.  
SEQ ID NO: 298 is the determined cDNA sequence for clone 25357.  
5 SEQ ID NO: 299 is the determined cDNA sequence for clone 25361.  
SEQ ID NO: 300 is the determined cDNA sequence for clone 25363.  
SEQ ID NO: 301 is the determined cDNA sequence for clone 25397.  
SEQ ID NO: 302 is the determined cDNA sequence for clone 25402.  
SEQ ID NO: 303 is the determined cDNA sequence for clone 25403.  
10 SEQ ID NO: 304 is the determined cDNA sequence for clone 25405.  
SEQ ID NO: 305 is the determined cDNA sequence for clone 25407.  
SEQ ID NO: 306 is the determined cDNA sequence for clone 25409.  
SEQ ID NO: 307 is the determined cDNA sequence for clone 25396.  
SEQ ID NO: 308 is the determined cDNA sequence for clone 25414.  
15 SEQ ID NO: 309 is the determined cDNA sequence for clone 25410.  
SEQ ID NO: 310 is the determined cDNA sequence for clone 25406.  
SEQ ID NO: 311 is the determined cDNA sequence for clone 25306.  
SEQ ID NO: 312 is the determined cDNA sequence for clone 25362.  
SEQ ID NO: 313 is the determined cDNA sequence for clone 25360.  
20 SEQ ID NO: 314 is the determined cDNA sequence for clone 25398.  
SEQ ID NO: 315 is the determined cDNA sequence for clone 25355.  
SEQ ID NO: 316 is the determined cDNA sequence for clone 25351.  
SEQ ID NO: 317 is the determined cDNA sequence for clone 25331.  
SEQ ID NO: 318 is the determined cDNA sequence for clone 25338.  
25 SEQ ID NO: 319 is the determined cDNA sequence for clone 25335.  
SEQ ID NO: 320 is the determined cDNA sequence for clone 25329.  
SEQ ID NO: 321 is the determined cDNA sequence for clone 25324.  
SEQ ID NO: 322 is the determined cDNA sequence for clone 25322.  
SEQ ID NO: 323 is the determined cDNA sequence for clone 25319.  
30 SEQ ID NO: 324 is the determined cDNA sequence for clone 25316.  
SEQ ID NO: 325 is the determined cDNA sequence for clone 25311.

- SEQ ID NO: 326 is the determined cDNA sequence for clone 25310.  
SEQ ID NO: 327 is the determined cDNA sequence for clone 25302.  
SEQ ID NO: 328 is the determined cDNA sequence for clone 25315.  
SEQ ID NO: 329 is the determined cDNA sequence for clone 25308.  
5 SEQ ID NO: 330 is the determined cDNA sequence for clone 25303.  
SEQ ID NO: 331-337 are the cDNA sequences of isoforms of the p53 tumor suppressor homologue, p63 (also referred to as L530S).  
SEQ ID NO: 338-344 are the amino acid sequences encoded by SEQ ID NO: 331-337, respectively.  
10 SEQ ID NO: 345 is a second cDNA sequence for the antigen L763P.  
SEQ ID NO: 346 is the amino acid sequence encoded by the sequence of SEQ ID NO: 345.  
SEQ ID NO: 347 is a determined full-length cDNA sequence for L523S.  
SEQ ID NO: 348 is the predicted amino acid sequence encoded by SEQ ID NO: 347.  
15 SEQ ID NO: 349 is the cDNA sequence encoding the N-terminal portion of L773P.  
SEQ ID NO: 350 is the amino acid sequence of the N-terminal portion of L773P.

#### DETAILED DESCRIPTION OF THE INVENTION

- As noted above, the present invention is generally directed to  
20 compositions and methods for the therapy and diagnosis of cancer, such as lung cancer.  
The compositions described herein may include lung tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic  
25 portion) of a lung tumor protein or a variant thereof. A "lung tumor protein" is a protein that is expressed in lung tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain lung tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western  
30 blot) with antisera of a patient afflicted with lung cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of

such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery human lung tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349.

#### LUNG TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a lung tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a lung tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a lung tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a lung tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the

encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native lung tumor protein or a portion thereof. The term "variants" also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20



positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

10 Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native lung tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; 15 followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal 20 homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous 25 genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. 30 For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that

is at least two fold greater in a lung tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and  
5 Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as lung tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

10 An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a lung tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be  
15 preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured  
20 bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using  
25 a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be  
30 generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs

may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding portions of lung tumor proteins are provided in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a lung tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a lung tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription

initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled  
5 with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*.  
10 Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

15 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation  
20 vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to  
25 permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not  
30 limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). ). The polynucleotides may also be administered as naked

plasmid vectors. Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

#### 15 LUNG TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a lung tumor protein or a variant thereof, as described herein. As noted above, a "lung tumor protein" is a protein that is expressed by lung tumor cells. Proteins that are lung tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with lung cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a lung tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may

contain a small N- and/or C-terminal deletion (e.g., 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-  
5 247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins).  
10 Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native lung tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is  
15 similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the  
20 sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

As noted above, a composition may comprise a variant of a native lung tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native lung tumor protein in one or more substitutions, deletions, additions  
25 and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above  
30 polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include

those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

5 Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the



polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression  
5 vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host  
10 cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or  
15 more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example,  
20 such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. *See* Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems  
25 Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known  
30 tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans,

or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second

polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997*).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible

for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see* 5 *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides 10 as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is 15 considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

#### BINDING AGENTS

The present invention further provides agents, such as antibodies and 20 antigen-binding fragments thereof, that specifically bind to a lung tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a lung tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a lung tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association 25 between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding 30 constant for complex formation exceeds about  $10^3$  L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as lung cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a lung tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum urine and/or tumor biopsies ) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically.

Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest  
5 may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as  
10 described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid  
15 cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

20 Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by  
25 conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be  
30 prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane,

*Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or  
5 more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria  
10 toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a  
15 substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an  
20 antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents,  
25 which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups,  
30 sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.



A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

### T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a lung tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a lung tumor polypeptide, polynucleotide encoding a lung tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a lung tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a lung tumor polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell

proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a lung tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a lung tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Lung tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a lung tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a lung tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a lung tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a lung tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

#### PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant

may be any substance that enhances or potentiates an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (e.g., polylactic galactide) and liposomes (into which the compound is incorporated; see e.g., Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl.*

*Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 5 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. 15 For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres 20 are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) 25 and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum 30 hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A,

*Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA);  
5 aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

10 Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- $\gamma$ , TNF $\alpha$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the  
15 induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using  
20 standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt.  
25 MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT) (see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555 and WO 99/33488. Immunostimulatory DNA sequences  
30 are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc.,

Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Other preferred adjuvants include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Ribi ImmunoChem Research Inc., Hamilton, MT), RC-529 (Ribi ImmunoChem Research Inc., Hamilton, MT) and Aminoalkyl glucosaminide 4-phosphates (AGPs).

Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology (*see, e.g.* Coombes et al., *Vaccine* 14:1429-1438, 1996) and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-co-glycolide), as well as polyacrylate, latex, starch, cellulose and dextran. Other delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally,

an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood,

bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a lung tumor protein (or portion or other variant thereof) such that the lung tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the lung tumor polypeptide, DNA



(naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Vaccines and pharmaceutical compositions may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a vaccine or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

#### CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as lung cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive

long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25  $\mu$ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free

survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a lung tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more lung tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as lung cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a lung tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent

that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length lung tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the

binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at  
5 A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody.  
10 Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

15 More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to  
20 bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.,* incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with lung cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of  
25 that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

30 Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second

antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide.

5 An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are  
10 generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of  
15 the reaction products.

To determine the presence or absence of a cancer, such as lung cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average  
20 mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical*  
25 *Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that  
30 encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered

positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

5 In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution  
10 containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent.  
15 Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the  
20 biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about  
25 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to  
30 those of ordinary skill in the art that the above protocols may be readily modified to use lung tumor polypeptides to detect antibodies that bind to such polypeptides in a



biological sample. The detection of such lung tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a lung tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a lung tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of lung tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a lung tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a lung tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (i.e., hybridizes to) a polynucleotide encoding the lung tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a lung tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%,

preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a lung tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the

level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor.

5 One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple lung tumor protein  
10 markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins  
15 provided herein may be combined with assays for other known tumor antigens.

#### DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components  
20 necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a lung tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements,  
25 such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a lung tumor protein in a biological sample. Such kits generally comprise at  
30 least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a lung tumor protein. Such an oligonucleotide may be used,

for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a lung tumor protein.

The following Examples are offered by way of illustration and not by  
5 way of limitation.

## EXAMPLE 1

ISOLATION AND CHARACTERIZATION OF cDNA SEQUENCES  
ENCODING LUNG TUMOR POLYPEPTIDES

5

This example illustrates the isolation of cDNA molecules encoding lung tumor-specific polypeptides from lung tumor cDNA libraries.

A. ISOLATION OF cDNA SEQUENCES FROM A LUNG SQUAMOUS CELL  
10 CARCINOMA LIBRARY

A human lung squamous cell carcinoma cDNA expression library was constructed from poly A<sup>+</sup> RNA from a pool of two patient tissues using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD) following the manufacturer's protocol. Specifically, lung carcinoma  
15 tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA was then purified using an oligo dT cellulose column as described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989. First-strand cDNA was  
20 synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with BstXI/EcoRI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with cDNA size fractionation columns (BRL Life Technologies), the cDNA was ligated into the BstXI/NotI site of pcDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life  
25 Technologies) by electroporation.

Using the same procedure, a normal human lung cDNA expression library was prepared from a pool of four tissue specimens. The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The lung  
30 squamous cell carcinoma library contained  $2.7 \times 10^6$  independent colonies, with 100% of clones having an insert and the average insert size being 2100 base pairs. The normal

lung cDNA library contained  $1.4 \times 10^6$  independent colonies, with 90% of clones having inserts and the average insert size being 1800 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA

5 cDNA library subtraction was performed using the above lung squamous cell carcinoma and normal lung cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a lung squamous cell carcinoma-specific subtracted cDNA library was generated as follows. Normal tissue cDNA library (80  $\mu$ g) was digested with BamHI and XhoI, followed by a filling-in  
10 reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 133  $\mu$ l of H<sub>2</sub>O, heat-denatured and mixed with 133  $\mu$ l (133  $\mu$ g) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (67  $\mu$ l) was added  
15 and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23  $\mu$ l H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10  $\mu$ g lung squamous cell carcinoma cDNA library was digested with NotI and SpeI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech, Palo Alto, CA). Typically, 5  $\mu$ g of  
20 cDNA was recovered after the sizing column. Following ethanol precipitation, the tracer DNA was dissolved in 5  $\mu$ l H<sub>2</sub>O. Tracer DNA was mixed with 15  $\mu$ l driver DNA and 20  $\mu$ l of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and  
25 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12  $\mu$ l H<sub>2</sub>O, mixed with 8  $\mu$ l driver DNA and 20  $\mu$ l of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After  
30 removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into NotI/SpeI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA) and

transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a lung squamous cell carcinoma specific subtracted cDNA library (herein after referred to as "lung subtraction I").

5 A second lung squamous cell carcinoma specific subtracted cDNA library (referred to as "lung subtraction II") was generated in a similar way to the lung subtraction library I, except that eight frequently recovered genes from lung subtraction I were included in the driver DNA, and 24,000 independent clones were recovered.

To analyze the subtracted cDNA libraries, plasmid DNA was prepared from 320 independent clones, randomly picked from the subtracted lung squamous cell carcinoma specific libraries. Representative cDNA clones were further characterized by  
10 DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). The cDNA sequences for sixty isolated clones are provided in SEQ ID NO: 1-60. These sequences were compared to known sequences in the gene bank using the EMBL and GenBank  
15 databases (release 96). No significant homologies were found to the sequences provided in SEQ ID NO: 2, 3, 19, 38 and 46. The sequences of SEQ ID NO: 1, 6-8, 10-13, 15, 17, 18, 20-27, 29, 30, 32, 34-37, 39-45, 47-49, 51, 52, 54, 55 and 57-59 were found to show some homology to previously identified expressed sequence tags (ESTs). The sequences of SEQ ID NO: 9, 28, 31 and 33 were found to show some homology to  
20 previously identified non-human gene sequences and the sequences of SEQ ID NO: 4, 5, 14, 50, 53, 56 and 60 were found to show some homology to gene sequences previously identified in humans.

The subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and the above normal  
25 lung tissue cDNA library and a cDNA library from normal liver and heart (constructed from a pool of one sample of each tissue as described above), plus twenty other cDNA clones that were frequently recovered in lung subtractions I and II, as the driver DNA (lung subtraction III). The normal liver and heart cDNA library contained  $1.76 \times 10^6$  independent colonies, with 100% of clones having inserts and the average insert size  
30 being 1600 base pairs. Ten additional clones were isolated (SEQ ID NO: 61-70). Comparison of these cDNA sequences with those in the gene bank as described above,

revealed no significant homologies to the sequences provided in SEQ ID NO: 62 and 67. The sequences of SEQ ID NO: 61, 63-66, 68 and 69 were found to show some homology to previously isolated ESTs and the sequence provided in SEQ ID NO: 70 was found to show some homology to a previously identified rat gene.

5           In further studies, the subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and a cDNA library from a pool of normal lung, kidney, colon, pancreas, brain, resting PBMC, heart, skin and esophagus as the driver DNA, with esophagus cDNAs making up one third of the driver material. Since esophagus is enriched in normal  
10   epithelial cells, including differentiated squamous cells, this procedure is likely to enrich genes that are tumor specific rather than tissues specific. The cDNA sequences of 48 clones determined in this subtraction are provided in SEQ ID NO: 177-224. The sequences of SEQ ID NO: 177, 178, 180, 181, 183, 187, 192, 195-197, 208, 211, 212, 215, 216, 218 and 219 showed some homology to previously identified genes. The  
15   sequences of SEQ ID NO: 179, 182, 184-186, 188-191, 193, 194, 198-207, 209 210, 213, 214, 217, 220 and 224 showed some homology to previously determined ESTs. The sequence of SEQ ID NO: 221-223 showed no homology to any previously determined sequence.

## 20   B.   ISOLATION   OF   cDNA   SEQUENCES   FROM   A   LUNG ADENOCARCINOMA LIBRARY

A human lung adenocarcinoma cDNA expression library was constructed as described above. The library contained  $3.2 \times 10^6$  independent colonies, with 100% of clones having an insert and the average insert size being 1500 base pairs.  
25   Library subtraction was performed as described above using the normal lung and normal liver and heart cDNA expression libraries described above as the driver DNA. Twenty-six hundred independent clones were recovered.

Initial cDNA sequence analysis from 100 independent clones revealed many ribosomal protein genes. The cDNA sequences for fifteen clones isolated in this  
30   subtraction are provided in SEQ ID NO: 71-86. Comparison of these sequences with those in the gene bank as described above revealed no significant homologies to the



sequence provided in SEQ ID NO: 84. The sequences of SEQ ID NO: 71, 73, 74, 77, 78 and 80-82 were found to show some homology to previously isolated ESTs, and the sequences of SEQ ID NO: 72, 75, 76, 79, 83 and 85 were found to show some homology to previously identified human genes.

5 In further studies, a cDNA library (referred to as mets3616A) was constructed from a metastatic lung adenocarcinoma. The determined cDNA sequences of 25 clones sequenced at random from this library are provided in SEQ ID NO: 255-279. The mets3616A cDNA library was subtracted against a cDNA library prepared from a pool of normal lung, liver, pancreas, skin, kidney, brain and resting PBMC. To  
10 increase the specificity of the subtraction, the driver was spiked with genes that were determined to be most abundant in the mets3616A cDNA library, such as EF1-alpha, integrin-beta and anticoagulant protein PP4, as well as with cDNAs that were previously found to be differentially expressed in subtracted lung adenocarcinoma cDNA libraries. The determined cDNA sequences of 51 clones isolated from the  
15 subtracted library (referred to as mets3616A-S1) are provided in SEQ ID NO: 280-330.

Comparison of the sequences of SEQ ID NO: 255-330 with those in the public databases revealed no significant homologies to the sequences of SEQ ID NO: 255-258, 260, 262-264, 270, 272, 275, 276, 279, 281, 287, 291, 296, 300 and 310. The sequences of SEQ ID NO: 259, 261, 265-269, 271, 273, 274, 277, 278, 282-285, 288-  
20 290, 292, 294, 297-299, 301, 303-309, 313, 314, 316, 320-324 and 326-330 showed some homology to previously identified gene sequences, while the sequences of SEQ ID NO: 280, 286, 293, 302, 310, 312, 315, 317-319 and 325 showed some homology to previously isolated expressed sequence tags (ESTs).

25

## EXAMPLE 2

### DETERMINATION OF TISSUE SPECIFICITY OF LUNG TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for seven  
30 representative lung tumor polypeptides described in Example 1 were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 2  $\mu$ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was used as an internal control for each of the tissues examined. 1  $\mu$ l of 1:30 dilution of cDNA was employed to enable the linear range amplification of the  $\beta$ -actin template and was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in five different types of tumor tissue (lung squamous cell carcinoma from 3 patients, lung adenocarcinoma, colon tumor from 2 patients, breast tumor and prostate tumor), and thirteen different normal tissues (lung from 4 donors, prostate, brain, kidney, liver, ovary, skeletal muscle, skin, small intestine, stomach, myocardium, retina and testes). Using a 10-fold amount of cDNA, the antigen LST-S1-90 (SEQ ID NO: 3) was found to be expressed at high levels in lung squamous cell carcinoma and in breast tumor, and at low to undetectable levels in the other tissues examined.

The antigen LST-S2-68 (SEQ ID NO: 15) appears to be specific to lung and breast tumor, however, expression was also detected in normal kidney. Antigens LST-S1-169 (SEQ ID NO: 6) and LST-S1-133 (SEQ ID NO: 5) appear to be very abundant in lung tissues (both normal and tumor), with the expression of these two genes being decreased in most of the normal tissues tested. Both LST-S1-169 and LST-S1-133 were also expressed in breast and colon tumors. Antigens LST-S1-6 (SEQ ID NO: 7) and LST-S2-12-5F (SEQ ID NO: 47) did not show tumor or tissue specific expression, with the expression of LST-S1-28 being rare and only detectable in a few tissues. The antigen LST-S3-7 (SEQ ID NO: 63) showed lung and breast tumor specific expression, with its message only being detected in normal testes when the PCR was performed for 30 cycles. Lower level expression was detected in some

normal tissues when the cycle number was increased to 35. Antigen LST-S3-13 (SEQ ID NO: 66) was found to be expressed in 3 out of 4 lung tumors, one breast tumor and both colon tumor samples. Its expression in normal tissues was lower compared to tumors, and was only detected in 1 out of 4 normal lung tissues and in normal tissues from kidney, ovary and retina. Expression of antigens LST-S3-4 (SEQ ID NO: 62) and LST-S3-14 (SEQ ID NO: 67) was rare and did not show any tissue or tumor specificity. Consistent with Northern blot analyses, the RT-PCT results on antigen LAT-S1-A-10A (SEQ ID NO: 78) suggested that its expression is high in lung, colon, stomach and small intestine tissues, including lung and colon tumors, whereas its expression was low or undetectable in other tissues.

A total of 2002 cDNA fragments isolated in lung subtractions I, II and III, described above, were colony PCR amplified and their mRNA expression levels in lung tumor, normal lung, and various other normal and tumor tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Seventeen non-redundant cDNA clones showed over-expression in lung squamous tumors, with expression in normal tissues tested (lung, skin, lymph node, colon, liver, pancreas, breast, heart, bone marrow, large intestine, kidney, stomach, brain, small intestine, bladder and salivary gland) being either undetectable, or 10-fold less compared to lung squamous tumors. The determined partial cDNA sequences for the clone L513S are provided in SEQ ID NO: 87 and 88; those for L514S are provided in SEQ ID NO: 89 and 90; those for L516S in SEQ ID NO: 91 and 92; that for L517S in SEQ ID NO: 93; that for L519S in SEQ ID NO: 94; those for L520S in SEQ ID NO: 95 and 96; those for L521S in SEQ ID NO: 97 and 98; that for L522S in SEQ ID NO: 99; that for L523S in SEQ ID NO: 100; that for L524S in SEQ ID NO: 101; that for L525S in SEQ ID NO: 102; that for L526S in SEQ ID NO: 103; that for L527S in SEQ ID NO: 104; that for L528S in SEQ ID NO: 105; that for L529S in SEQ ID NO: 106;

and those for L530S in SEQ ID NO: 107 and 108. Additionally, the full-length cDNA sequence for L530S is provided in SEQ ID NO: 151, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 152. L530S shows homology to a splice variant of a p53 tumor suppressor homologue, p63. The cDNA sequences of 7  
5 known isoforms of p63 are provided in SEQ ID NO: 331-337, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 338-344, respectively.

Due to polymorphisms, the clone L531S appears to have two forms. A first determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 109, with the corresponding predicted amino acid sequence being provided in SEQ ID NO:  
10 110. A second determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 111, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 112. The sequence of SEQ ID NO: 111 is identical to that of SEQ ID NO: 109, except that it contains a 27 bp insertion. Similarly, L514S also has two alternatively spliced forms; the first variant cDNA is listed as SEQ ID NO: 153, with  
15 the corresponding amino acid sequence being provided in SEQ ID NO: 155. The second variant form of L514S full-length cDNA is provided in SEQ ID NO: 154, with its corresponding amino acid sequence being provided in SEQ ID NO: 156.

Full length cloning for L524S (SEQ ID NO: 101) yielded two variants (SEQ ID NO: 163 and 164) with the corresponding predicted amino acid sequences of  
20 SEQ ID NO: 165 and 166, respectively. Both variants have been shown to encode parathyroid hormone-related peptide.

Attempts to isolate the full-length cDNA for L519S, resulted in the isolation of the extended cDNA sequence provided in SEQ ID NO: 173, which contains a potential open reading frame. The predicted amino acid sequence encoded by the  
25 sequence of SEQ ID NO: 173 is provided in SEQ ID NO: 174. Additionally, the full-length cDNA sequence for the clone of SEQ ID NO: 100 (known as L523S), a known gene, is provided in SEQ ID NO: 175, with the corresponding predicted amino acid sequence provided in SEQ ID NO: 176. In further studies, a full-length cDNA sequence for L523S was isolated from a L523S-positive tumor cDNA library by PCR  
30 amplification using gene specific primers designed from the sequence of SEQ ID NO: 175. The determined cDNA sequence is provided in SEQ ID NO: \*\*. The amino acid

sequence encoded by this sequence is provided in SEQ ID NO: \*\*. This protein sequence differs from the previously published protein sequence at two amino acid positions, namely at positions 158 and 410.

Comparison of the sequences of L514S and L531S (SEQ ID NO: 87 and 88, 89 and 90, and 109, respectively) with those in the gene bank, as described above, revealed no significant homologies to known sequences. The sequences of L513S, L516S, L517S, L519S, L520S and L530S (SEQ ID NO: 87 and 88, 91 and 92, 93, 94, 95 and 96, 107 and 108, respectively) were found to show some homology to previously identified ESTs. The sequences of L521S, L522S, L523S, L524S, L525S, L526S, L527S, L528S and L529S (SEQ ID NO: 97 and 98, 99, 99, 101, 102, 103, 104, 105, and 106, respectively) were found to represent known genes. The determined full-length cDNA sequences for L520S is provided in SEQ ID NO: 113, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 114. Subsequent microarray analysis has shown L520S to be overexpressed in breast tumors in addition to lung squamous tumors.

Further analysis has demonstrated that L529S (SEQ ID NO: 106 and 115), L525S (SEQ ID NO: 102 and 120) and L527S (SEQ ID NO: 104) are cytoskeletal components and potentially squamous cell specific proteins. L529S is connexin 26, a gap junction protein. It is highly expressed in lung squamous tumor 9688T, and moderately over-expressed in two others. However, lower level expression of connexin 26 is also detectable in normal skin, colon, liver and stomach. The over-expression of connexin 26 in some breast tumors has been reported and a mutated form of L529S may result in over-expression in lung tumors. L525S is plakophilin 1, a desmosomal protein found in plaque-bearing adhering junctions of the skin. Expression levels for L525S mRNA is highly elevated in three out of four lung squamous tumors tested, and in normal skin. L527S has been identified as keratin 6 isoform, type II 58 Kd keratin, and cytokeratin 13 and shows over-expression in squamous tumors and low expression in normal skin, breast and colon tissues. Notably, keratin and keratin-related genes have been extensively documented as potential markers for lung cancer including CYFRA2.1 (Pastor, A., et al, *Eur. Respir. J.*, 10:603-609, 1997). L513S (SEQ ID NO: 87 and 88)

shows moderate over-expression in several tumor tissues tested, and encodes a protein that was first isolated as a pemphigus vulgaris antigen.

L520S (SEQ ID NO: 95 and 96) and L521S (SEQ ID NO: 97 and 98) are highly expressed in lung squamous tumors, and L520S is up-regulated in normal salivary gland and L521S is over-expressed in normal skin. Both belong to a family of small proline rich proteins and represent markers for fully differentiated squamous cells. L521S has been described as a specific marker for lung squamous tumor (Hu, R., et al, *Lung Cancer*, 20:25-30, 1998). L515S (SEQ ID NO: 162) encodes IGF- $\beta$ 2 and L516S is an aldose reductase homologue and both are moderately expressed in lung squamous tumors and in normal colon. Notably, L516S (SEQ ID NO: 91 and 92) is up-regulated in metastatic tumors but not primary lung adenocarcinoma, an indication of its potential role in metatasis and a potential prognostic marker. L522S (SEQ ID NO: 99) is moderately over-expressed in lung squamous tumors with minimum expression in normal tissues. L522S has been shown to belong to a class IV alcohol dehydrogenase, ADH7, and its expression profile suggests it is a squamous cell specific antigen. L523S (SEQ ID NO: 100) is moderately over-expressed in lung squamous tumor, human pancreatic cancer cell lines and pancreatic cancer tissues, suggesting this gene may be a shared antigen between pancreatic and lung squamous cell cancer.

L524S (SEQ ID NO: 101) is over-expressed in the majority of squamous tumors tested and is homologous with parathyroid hormone-related peptide (PTHrP), which is best known to cause humoral hypercalcaemia associated with malignant tumors such as leukemia, prostate and breast cancer. It is also believed that PTHrP is most commonly associated with squamous carcinoma of lung and rarely with lung adenocarcinoma (Davidson, L.A., et al, *J. Pathol.*, 178: 398-401, 1996). L528S (SEQ ID NO: 105) is highly over-expressed in two lung squamous tumors with moderate expression in two other squamous tumors, one lung adenocarcinoma and some normal tissues, including skin, lymph nodes, heart, stomach and lung. It encodes the NMB gene that is similar to the precursor of melanocyte specific gene Pmel17, which is reported to be preferentially expressed in low-metastatic potential melanoma cell lines. This suggests that L528S may be a shared antigen in both melanoma and lung squamous cell carcinoma. L526S (SEQ ID NO: 103) is overexpressed in all lung

squamous cell tumor tissues tested and has been shown to share homology with a gene (ATM) in which a mutation causes ataxia telangiectasia, a genetic disorder in humans causing a predisposition to cancer, among other symptoms. ATM encodes a protein that activates p53 mediated cell-cycle checkpoint through direct binding and phosphorylation of the p53 molecule. Approximately 40% of lung cancer is associated with p53 mutations, and it is speculated that over-expression of ATM is a result of compensation for loss of p53 function, but it is unknown whether over-expression is the cause of result of lung squamous cell carcinoma. Additionally, expression of L526S (ATM) is also detected in a metastatic but not lung adenocarcinoma, suggesting a role in metastasis.

Expression of L523S (SEQ ID NO: 175), was also examined by real time RT-PCR as described above. In a first study using a panel of lung squamous tumors, L523S was found to be expressed in 4/7 lung squamous tumors, 2/3 head and neck squamous tumors and 2/2 lung adenocarcinomas, with low level expression being observed in skeletal muscle, soft palate and tonsil. In a second study using a lung adenocarcinoma panel, expression of L523S was observed in 4/9 primary adenocarcinomas, 2/2 lung pleural effusions, 1/1 metastatic lung adenocarcinomas and 2/2 lung squamous tumors, with little expression being observed in normal tissues.

Expression of L523S in lung tumors and various normal tissues was also examined by Northern blot analysis, using standard techniques. In a first study, L523S was found to be expressed in a number of lung adenocarcinomas and squamous cell carcinomas, as well as normal tonsil. No expression was observed in normal lung. In a second study using a normal tissue blot (HB-12) from Clontech, no expression was observed in brain, skeletal muscle, colon, thymus, spleen, kidney, liver, small intestine, lung or PBMC, although there was strong expression in placenta.

### EXAMPLE 3

#### ISOLATION AND CHARACTERIZATION OF LUNG TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

Eight hundred and fifty seven clones from a cDNA subtraction library, containing cDNA from a pool of two human lung squamous tumors subtracted against eight normal human tissue cDNAs including lung, PBMC, brain, heart, kidney, liver, pancreas, and skin, (Clontech, Palo Alto, CA) were derived and submitted to a first  
5 round of PCR amplification. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector P7- Adv vector (Clontech, Palo Alto, CA) and transformed into DH5 $\alpha$  *E. coli* (Gibco, BRL). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated  
10 Sequencer Model 373A.

One hundred and sixty two positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the the EMBL and GenBank databases, as described above, revealed no significant homologies to 13 of these clones, hereinafter referred to as Contigs 13, 16, 17, 19, 22, 24, 29, 47, 49, 56-59. The  
15 determined cDNA sequences for these clones are provided in SEQ ID NO: 125, 127-129, 131-133, 142, 144, 148-150, and 157, respectively. Contigs 1, 3-5, 7-10, 12, 11, 15, 20, 31, 33, 38, 39, 41, 43, 44, 45, 48, 50, 53, 54 (SEQ ID NO: 115-124, 126, 130, 134-141, 143, 145-147, respectively) were found to show some degree of homology to previously identified DNA sequences. Contig 57 (SEQ ID NO: 149) was found to  
20 represent the clone L519S (SEQ ID NO: 94) disclosed in US. Patent Application No. 09/123,912, filed July 27, 1998. To the best of the inventors' knowledge, none of these sequences have been previously shown to be differentially over-expressed in lung tumors.

mRNA expression levels for representative clones in lung tumor tissues,  
25 normal lung tissues (n=4), resting PBMC, salivary gland, heart, stomach, lymph nodes, skeletal muscle, soft palate, small intestine, large intestine, bronchial, bladder, tonsil, kidney, esophagus, bone marrow, colon, adrenal gland, pancreas, and skin, (all derived from human) were determined by RT-PCR as described above. Expression levels using microarray technology, as described above, were examined in one sample of each tissue  
30 type unless otherwise indicated.



Contig 3 (SEQ ID NO: 116) was found to be highly expressed in all head and neck squamous cell tumors tested (17/17), and expressed in the majority (8/12) of lung squamous tumors, (high expression in 7/12, moderate in 2/12, and low in 2/12), while showing negative expression for 2/4 normal lung tissues and low expression in the remaining two samples. Contig 3 showed moderate expression in skin and soft palate, and lowered expression levels in resting PBMC, large intestine, salivary gland, tonsil, pancreas, esophagus, and colon. Contig 11 (SEQ ID NO: 124) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 14/17, and moderately expressed in 3/17. Additionally, expression in lung squamous tumors showed high expression in 3/12 and moderate in 4/12. Contig 11 was negative for 3/4 normal lung samples, with the remaining sample having only low expression. Contig 11 showed low to moderate reactivity to salivary gland, soft palate, bladder, tonsil, skin, esophagus, and large intestine. Contig 13 (SEQ ID NO: 125) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 12/17, and moderately expressed in 5/17. Contig 13 was expressed in 7/12 lung squamous tumors, with high expression in 4/12 and moderate expression in three samples. Analysis of normal lung samples showed negative expression for 2/4 and low to moderate expression in the remaining two samples. Contig 13 did show low to moderate reactivity to resting PBMC, salivary gland, bladder, pancreas, tonsil, skin, esophagus, and large intestine, as well as high expression in soft palate. Contig 16 (SEQ ID NO: 127) was found to be moderately expressed in some head and neck squamous cell tumors (6/17) and one lung squamous tumor; while showing no expression in any normal lung samples tested. Contig 16 did show low reactivity to resting PBMC, large intestine, skin, salivary gland, and soft palate. Contig 17 (SEQ ID NO: 128) was shown to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 5/17, and moderately expressed in 12/17. Expression levels in lung squamous tumors showed one tumor sample with high expression and 3/12 with moderate levels. Contig 17 was negative for 2/4 normal lung samples, with the remaining samples having only low expression. Additionally, low level expression was found in esophagus and soft palate. Contig 19 (SEQ ID NO: 129) was found to be expressed in most head and neck squamous cell tumors tested (11/17); with two

samples having high levels, 6/17 showing moderate expression, and low expression being found in 3/17. Testing in lung squamous tumors revealed only moderate expression in 3/12 samples. Expression levels in 2/4 of normal lung samples were negative, the two other samples having only low expression. Contig 19 showed low expression levels in esophagus, resting PBMC, salivary gland, bladder, soft palate and pancreas.

Contig 22 (SEQ ID NO: 131), was shown to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in four of these samples, moderate expression in 6/17, and low expression in 3/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression in two normal lung samples and low expression in two other samples (n=4). Contig 22 showed low expression in skin, salivary gland and soft palate. Similarly, Contig 24 (SEQ ID NO: 132) was found to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in three of these samples, moderate expression in 6/17, and low expression in 4/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression for three normal lung samples and low expression in one sample (n=4). Contig 24 showed low expression in skin, salivary gland and soft palate. Contig 29 (SEQ ID NO: 133) was expressed in nearly all head and neck squamous cell tumors tested (16/17): highly expressed in 4/17, moderately expressed in 11/17, with low expression in one sample. Also, it was moderately expressed in 3/12 lung squamous tumors, while being negative for 2/4 normal lung samples. Contig 29 showed low to moderate expression in large intestine, skin, salivary gland, pancreas, tonsil, heart and soft palate. Contig 47 (SEQ ID NO: 142) was expressed in most head and neck squamous cell tumors tested (12/17): moderate expression in 10/17, and low expression in two samples. In lung squamous tumors, it was highly expressed in one sample and moderately expressed in two others (n=13). Contig 47 was negative for 2/4 normal lung samples, with the remaining two samples having moderate expression. Also, Contig 47 showed moderate expression in large intestine, and pancreas, and low expression in skin, salivary gland, soft palate, stomach, bladder, resting PBMC, and tonsil.

Contig 48 (SEQ ID NO: 143) was expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 8/17 and moderately expressed in 7/17, with low expression in two samples. Expression levels in lung squamous tumors were high to moderate in three samples (n=13). Contig 48 was negative for one out of four normal lung samples, the remaining showing low or moderate expression. Contig 48 showed moderate expression in soft palate, large intestine, pancreas, and bladder, and low expression in esophagus, salivary gland, resting PBMC, and heart. Contig 49 (SEQ ID NO: 144) was expressed at low to moderate levels in 6/17 head and neck squamous cell tumors tested. Expression levels in lung squamous tumors were moderate in three samples (n=13). Contig 49 was negative for 2/4 normal lung samples, the remaining samples showing low expression. Moderate expression levels in skin, salivary gland, large intestine, pancreas, bladder and resting PBMC were shown, as well as low expression in soft palate, lymph nodes, and tonsil. Contig 56 (SEQ ID NO: 148) was expressed in low to moderate levels in 3/17 head and neck squamous cell tumors tested, and in lung squamous tumors, showing low to moderate levels in three out of thirteen samples. Notably, low expression levels were detected in one adenocarcinoma lung tumor sample (n=2). Contig 56 was negative for 3/4 normal lung samples, and showed moderate expression levels in only large intestine, and low expression in salivary gland, soft palate, pancreas, bladder, and resting PBMC. Contig 58, also known as L769P, (SEQ ID NO: 150) was expressed at moderate levels in 11/17 head and neck squamous cell tumors tested and low expression in one additional sample. Expression in lung squamous tumors showed low to moderate levels in three out of thirteen samples. Contig 58 was negative for 3/4 normal lung samples, with one sample having low expression. Moderate expression levels in skin, large intestine, and resting PBMC were demonstrated, as well as low expression in salivary gland, soft palate, pancreas, and bladder. Contig 59 (SEQ ID NO: 157) was expressed in some head, neck, and lung squamous tumors. Low level expression of Contig 59 was also detected in salivary gland and large intestine.

The full-length cDNA sequence for Contig 22, also referred to as L763P, is provided in SEQ ID NO: 158, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 159. Real-time RT-PCR analysis of L763P revealed

that it is highly expressed in 3/4 lung squamous tumors as well as 4/4 head and neck squamous tumors, with low level expression being observed in normal brain, skin, soft pallet and trachea. Subsequent database searches revealed that the sequence of SEQ ID NO: 158 contains a mutation, resulting in a frameshift in the corresponding protein sequence. A second cDNA sequence for L763P is provided in SEQ ID NO: 345, with the corresponding amino acid sequence being provided in SEQ ID NO: 346. The sequences of SEQ ID NO: 159 and 346 are identical with the exception of the C-terminal 33 amino acids of SEQ ID NO: 159.

The full-length cDNA sequence incorporating Contigs 17, 19, and 24, referred to as L762P, is provided in SEQ ID NO: 160, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 161. Further analysis of L762P has determined it to be a type I membrane protein and two additional variants have been sequenced. Variant 1 (SEQ ID NO: 167, with the corresponding amino acid sequence in SEQ ID NO: 169) is an alternatively spliced form of SEQ ID NO: 160 resulting in deletion of 503 nucleotides, as well as deletion of a short segment of the expressed protein. Variant 2 (SEQ ID NO: 168, with the corresponding amino acid sequence in SEQ ID NO: 170) has a two nucleotide deletion at the 3' coding region in comparison to SEQ ID NO: 160, resulting in a secreted form of the expressed protein. Real-time RT-PCR analysis of L762P revealed that is over-expressed in 3/4 lung squamous tumors and 4/4 head & neck tumors, with low level expression being observed in normal skin, soft pallet and trachea.

The full-length cDNA sequence for contig 56 (SEQ ID NO: 148), also referred to as L773P, is provided in SEQ ID NO: 171, with the predicted amino acid sequence in SEQ ID NO: 172. L773P was found to be identical to dihydroxyl dehydrogenase at the 3' portion of the gene, with divergent 5' sequence. As a result, the 69 N-terminal amino acids are unique. The cDNA sequence encoding the 69 N-terminal amino acids is provided in SEQ ID NO: 349, with the N-terminal amino acid sequence being provided in SEQ ID NO: 350. Real-time PCR revealed that L773P is highly expressed in lung squamous tumor and lung adenocarcinoma, with no detectable expression in normal tissues. Subsequent Northern blot analysis of L773P demonstrated that this transcript is differentially over-expressed in squamous tumors

and detected at approximately 1.6 Kb in primary lung tumor tissue and approximately 1.3 Kb in primary head and neck tumor tissue.

Subsequent microarray analysis has shown Contig 58, also referred to as L769S (SEQ ID NO: 150), to be overexpressed in breast tumors in addition to lung squamous tumors.

#### EXAMPLE 4

##### SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

#### EXAMPLE 5

##### PREPARATION OF ANTIBODIES AGAINST LUNG CANCER ANTIGENS

Polyclonal antibodies against the lung cancer antigens L514S, L528S and L531S (SEQ ID NO: 155, 225 and 112, respectively) were prepared as follows.

Rabbits were immunized with recombinant protein expressed in and purified from *E. coli* as described above. For the initial immunization, 400 µg of

antigen combined with muramyl dipeptide (MDP) was injected subcutaneously (S.C.). Animals were boosted S.C. 4 weeks later with 200 µg of antigen mixed with incomplete Freund's Adjuvant (IFA). Subsequent boosts of 100 µg of antigen mixed with IFA were injected S.C. as necessary to induce high antibody titer responses. Serum bleeds from immunized rabbits were tested for antigen-specific reactivity using ELISA assays with purified protein. Polyclonal antibodies against L514S, L528S and L531S were affinity purified from high titer polyclonal sera using purified protein attached to a solid support.

Immunohistochemical analysis using polyclonal antibodies against L514S was performed on a panel of 5 lung tumor samples, 5 normal lung tissue samples and normal colon, kidney, liver, brain and bone marrow. Specifically, tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with antibody for 1 hr. HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize L514S immunoreactivity. L514S was found to be highly expressed in lung tumor tissue with little or no expression being observed in normal lung, brain or bone marrow. Light staining was observed in colon and kidney. Staining was seen in normal liver but no mRNA has been detected in this tissue making this result suspect.

## EXAMPLE 6

### PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

Immunogenic peptides from the lung cancer antigen L762P (SEQ ID NO: 161) for HLA-A2/K<sup>b</sup>-restricted CD8<sup>+</sup> T cells were identified as follows.

The location of HLA-A2 binding peptides within the lung cancer antigen L762P (SEQ ID NO: 161) was predicted using a computer program which predicts peptides sequences likely to be to HLA-A\*0201 by fitting to the known peptide binding motif for HLA-A\*0201 (Rupert *et al.* (1993) *Cell* 74:929; Rammensee *et al.* (1995) *Immunogenetics* 41:178-228). A series of 19 synthetic peptides corresponding to a selected subset of the predicted HLA-A\*0201 binding peptides was prepared as described above.

Mice expressing the transgene for human HLA A2/K<sup>b</sup> (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with the synthetic peptides, as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 50µg of L726P peptide and 120µg of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared. Cells were then resuspended at 7 x 10<sup>6</sup> cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10<sup>-5</sup> M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) L762P peptide- (5µg/ml) and 10mg/ml B<sub>2</sub>-microglobulin- (3 µg/ml) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). After six days, cells (5 x 10<sup>5</sup>/ml) were restimulated with 2.5 x 10<sup>6</sup>/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 5 x 10<sup>6</sup>/ml irradiated (3000 rads) A2/K<sup>b</sup>-transgenic spleen feeder cells. Cells were cultured in the presence of 10U/ml IL-2. Cells were restimulated on a weekly basis as described, in preparation for cloning the line.

Peptide-specific cell lines were cloned by limiting dilution analysis with irradiated (20,000 rads) L762P peptide-pulsed EL4 A2Kb tumor cells (1 x 10<sup>4</sup> cells/well) as stimulators and irradiated (3000 rads) A2/K<sup>b</sup>-transgenic spleen cells as feeders (5 x 10<sup>5</sup> cells/ well) grown in the presence of 10U/ml IL-2. On day 7, cells were restimulated as before. On day 14, clones that were growing were isolated and maintained in culture.

Cell lines specific for L762P-87 (SEQ ID NO: 226; corresponding to amino acids 87-95 of SEQ ID NO: 161), L726P-145 (SEQ ID NO: 227; corresponding to amino acids 145-153 of SEQ ID NO: 161), L726P-585 (SEQ ID NO: 228; corresponding to amino acids 585-593 of SEQ ID NO: 161), L762P-425 (SEQ ID NO: 229; corresponding to amino acids 425-433 of SEQ ID NO: 161), L762P(10)-424 (SEQ ID NO: 230; corresponding to amino acids 424-433 of SEQ ID NO: 161) and L762P(10)-458 (SEQ ID NO: 231; corresponding to amino acids 458-467 of SEQ ID

NO: 161) demonstrated significantly higher reactivity (as measured by percent specific lysis) against L762P peptide-pulsed EL4-A2/K<sup>b</sup> tumor target cells than control peptide-pulsed EL4-A2/K<sup>b</sup> tumor target cells.

#### EXAMPLE 7

##### IDENTIFICATION OF CD4 IMMUNOGENIC T CELL EPITOPES DERIVED FROM THE LUNG CANCER ANTIGEN L762P

CD4 T cell lines specific for the antigen L762P (SEQ ID NO: 161) were  
10 generated as follows.

A series of 28 overlapping peptides were synthesized that spanned approximately 50% of the L762P sequence. For priming, peptides were combined into pools of 4-5 peptides, pulsed at 20 micrograms/ml into dendritic cells for 24 hours. The dendritic cells were then washed and mixed with positively selected CD4<sup>+</sup> T cells in 96  
15 well U-bottomed plates. Forty cultures were generated for each peptide pool. Cultures were restimulated weekly with fresh dendritic cells loaded with peptide pools. Following a total of 3 stimulation cycles, cells were rested for an additional week and tested for specificity to antigen presenting cells (APC) pulsed with peptide pools using interferon-gamma ELISA and proliferation assays. For these assays, adherent  
20 monocytes loaded with either the relevant peptide pool or an irrelevant peptide were used as APC. T cell lines that appeared to specifically recognize L762P peptide pools both by cytokine release and proliferation were identified for each pool. Emphasis was placed on identifying T cells with proliferative responses. T cell lines that demonstrated either both L762P-specific cytokine secretion and proliferation, or strong proliferation  
25 alone were further expanded to be tested for recognition of individual peptides from the pools, as well as for recognition of recombinant L762P. The source of recombinant L762P was *E. coli*, and the material was partially purified and endotoxin positive. These studies employed 10 micrograms of individual peptides, 10 or 2 micrograms of an irrelevant peptide, and 2 or 0.5 micrograms of either L762P protein or an irrelevant,  
30 equally impure, *E. coli* generated recombinant protein. Significant interferon-gamma production and CD4 T cell proliferation was induced by a number of L762P-derived



peptides in each pool. The amino acid sequences for these peptides are provided in SEQ ID NO: 232-251. These peptides correspond to amino acids 661-680, 676-696, 526-545, 874-893, 811-830, 871-891, 856-875, 826-845, 795-815, 736-755, 706-725, 706-725, 691-710, 601-620, 571-590, 556-575, 616-635, 646-665, 631-650, 541-560  
5 and 586-605, respectively, of SEQ ID NO: 161.

CD4 T cell lines that demonstrated specificity for individual L762P-derived peptides were further expanded by stimulation with the relevant peptide at 10 micrograms/ml. Two weeks post-stimulation, T cell lines were tested using both proliferation and IFN-gamma ELISA assays for recognition of the specific peptide. A  
10 number of previously identified T cells continued to demonstrate L762P-peptide specific activity. Each of these lines was further expanded on the relevant peptide and, following two weeks of expansion, tested for specific recognition of the L762P-peptide in titration experiments, as well as for recognition of recombinant *E. coli*-derived L762P protein. For these experiments, autologous adherent monocytes were pulsed with either  
15 the relevant L762P-derived peptide, an irrelevant mammaglobin-derived peptide, recombinant *E. coli*-derived L762P (approx. 50% pure), or an irrelevant *E. coli*-derived protein. The majority of T cell lines were found to show low affinity for the relevant peptide, since specific proliferation and IFN-gamma ratios dramatically decreased as L762P peptide was diluted. However, four lines were identified that demonstrated  
20 significant activity even at 0.1 micrograms/ml peptide. Each of these lines (referred to as A/D5, D/F5, E/A7 and E/B6) also appeared to specifically proliferate in response to the *E. coli*-derived L762P protein preparation, but not in response to the irrelevant protein preparation. The amino acid sequences of the L762P-derived peptides recognized by these lines are provided in SEQ ID NO: 234, 249, 236 and 245,  
25 respectively. No protein specific IFN-gamma was detected for any of the lines. Lines A/D5, E/A7 and E/B6 were cloned on autologous adherent monocytes pulsed with the relevant peptide at 0.1 (A/D5 and E/A7) or 1 (D/F5) microgram/ml. Following growth, clones were tested for specificity for the relevant peptide. Numerous clones specific for the relevant peptide were identified for lines A/D5 and E/A7.

## EXAMPLE 8

## PROTEIN EXPRESSION OF LUNG TUMOR-SPECIFIC ANTIGENS

5 a) Expression of L514S in *E. coli*

The lung tumor antigen L514S (SEQ ID NO: 89) was subcloned into the expression vector pE32b at NcoI and NotI sites, and transformed into *E. coli* using standard techniques. The protein was expressed from residues 3-153 of SEQ ID NO: 89. The expressed amino acid sequence and the corresponding DNA sequence are  
10 provided in SEQ ID NO: 252 and 253, respectively.

b) Expression of L762P

Amino acids 32-944 of the lung tumor antigen L762P (SEQ ID NO: 161), with a 6X His Tag, were subcloned into a modified pET28 expression vector,  
15 using kanamycin resistance, and transformed into BL21 CodonPlus using standard techniques. Low to moderate levels of expression were observed. The determined DNA sequence of the L762P expression construct is provided in SEQ ID NO: 254.

From the foregoing it will be appreciated that, although specific  
20 embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

## CLAIMS

1. An isolated polypeptide, comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) sequences recited in SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349;
- (b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 under moderately stringent conditions; and
- (c) complements of sequences of (a) or (b).
2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158,

160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences.

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3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 110, 112, 114, 152, 155, 156, 159, 161, 165, 166, 169, 170, 172, 174, 176, 226-252, 346, 348 and 350.

4. An isolated polynucleotide encoding at least 15 amino acid  
10 residues of a lung tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29,  
15 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a  
20 complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO:  
25 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317,  
30 323, 345, 347 and 349 or a complement of any of the foregoing sequences.

6. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349.
7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 under moderately stringent conditions.
8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.
9. An expression vector, comprising a polynucleotide according to any one of claims claim 4-8.
10. A host cell transformed or transfected with an expression vector according to claim 9.
11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a lung tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84,

86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and  
5 349\_or a complement of any of the foregoing polynucleotide sequences.

12. A fusion protein, comprising at least one polypeptide according to claim 1.

10 13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

14. A fusion protein according to claim 12, wherein the fusion  
15 protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

20 16. An isolated polynucleotide encoding a fusion protein according to claim 12.

17. A pharmaceutical composition, comprising a physiologically  
25 acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- 30 (e) a polynucleotide according to claim 16.

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.

20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 18.

23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

5 (a) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171,  
10 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii);  
in combination with an immunostimulant.

15 26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.

27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

20

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient,  
25 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

30 (a) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and



349;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii) encoded by a polynucleotide recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349; and thereby inhibiting the development of a cancer in the patient.

30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is lung cancer.

32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349; and

(ii) complements of the foregoing polynucleotides; wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

33. A method according to claim 32, wherein the biological sample is blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.

5

35. A method for stimulating and/or expanding T cells specific for a lung tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

(a) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(ii) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(iii) complements of sequences of (i) or (ii);

(b) polynucleotides encoding a polypeptide of (a); and

(c) antigen presenting cells that express a polypeptide of (a);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

25

36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

30

38. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

5 (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

10 (1) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

15 (3) complements of sequences of (1) or (2);  
(ii) polynucleotides encoding a polypeptide of (i); and  
(iii) antigen presenting cells that expresses a polypeptide of  
20 (i);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

25 39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

30 (i) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence

selected from the group consisting of:

- (1) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;
- 5 (2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and
- (3) complements of sequences of (1) or (2);
- 10 (ii) polynucleotides encoding a polypeptide of (i); and
- (iii) antigen presenting cells that express a polypeptide of (i);
- such that T cells proliferate;
- (b) cloning at least one proliferated cell to provide cloned T cells;
- and
- 15 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 20 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 or a complement of any of the
- 25 foregoing polynucleotide sequences;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

30

41. A method according to claim 40, wherein the binding agent is an

antibody.

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

43. A method according to claim 40, wherein the cancer is lung cancer.

44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

45. A method according to claim 44, wherein the binding agent is an antibody.

46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

47. A method according to claim 44, wherein the cancer is a lung

cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

5 (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347  
10 and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the  
15 presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

20

50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

25

51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a  
30 polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347

and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

(a) one or more antibodies according to claim 11; and

(b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

57. A kit according to claim 54, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing polynucleotides.

59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349.

20

60. A diagnostic kit, comprising:

- (a) an oligonucleotide according to claim 59; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

25



## SEQUENCE LISTING

<110> Corixa Corporation et al.

<120> COMPOUNDS AND METHODS FOR THERAPY  
AND DIAGNOSIS OF LUNG CANCER

<130> 210121.45501PC

<140> PCT

<141> 2000-04-03

<160> 350

<170> FastSEQ for Windows Version 3.0

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<211> 315

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<213> Homo sapien

<220>

<221> misc\_feature

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<223> n = A,T,C or G

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gcagagacag actggtggtt gaacctggag gtgccaaaaa agccagctgc gggcccagga	60
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ttcatctcca gcagagacaa cggaggaggc tcccaccagg acggttctca ttatttatat	180
gttaatatgt ttgtaaacct atgtacagtt ttttttgggg gggaagcaat gggaanggta	240
naaattacaa atagaatcat ttgctgtaat ccttaaattg caaacggtca ggccacgtga	300
aaaaaaaaaa aaaaaa	315

<210> 2

<211> 380

<212> DNA

<213> Homo sapien

<400> 2

atntaggtt aagattttgt ttacccttgt tactaaggag caaattagta ttaaagtata	60
atatatataa acaaatacaa aaagttttga gtggttcagc ttttttattt tttttaatgg	120
cataactttt aacaacactg ctctgtaatg ggttgaactg tggtagctag actgagataa	180
ctgaaatgag tggatgtata gtgttattgc ataattatcc cactatgaag caaagggact	240
ggataaattc ccagtctaga ttattagcct ttgttaacca tcaagcacct agaagaagaa	300
ttattggaaa ttttgtcctc tgtaactggc actttggggg gtgacttate ttttgccttt	360
gtaaaaaaaa aaaaaaaaaa	380

<210> 3

<211> 346

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<220>  
 <221> misc\_feature  
 <222> (1)...(346)  
 <223> n = A,T,C or G

<400> 3  
 ttgtaagtat acaatttttag aaaggattaa atgttattga tcattttact gaatactgca 60  
 catcctcacc atacaccatc cactttccaa taacatttaa tcctttctaa aattgtaagt 120  
 atacaattgt actttctttg gattttcata acaaataac catagactgt taattttatt 180  
 gaagtttcct taatggaatg agtcattttt gtcttggtgt tttgaggta cctttgcttt 240  
 gacttccaac aattgatca tatagtgtg agctgtggaa atctttaagt ttattctata 300  
 gcaataaatt ctattnnnag annccngggn naaaannann annaaa 346

<210> 4  
 <211> 372  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(372)  
 <223> n = A,T,C or G

<400> 4  
 actagtctca ttactccaga attatgctct tgtacctgtg tggctgggtt tcttagtcgt 60  
 tggtttgggt tggttttttg aactggtatg taggggtggt caccagttcta atgtaagcac 120  
 tctcttctcc aagttgtgct ttgtggggac aatcattctt tgaacattag agaggaaggc 180  
 agttcaagct gttgaaaaga ctattgctta tttttgtttt taaagacctt cttgacgtca 240  
 tgtggacagt gcacgtgcct tacgctacat cttgttttct aggaagaagg ggatgcnggg 300  
 aaggantggg tgctttgtga tggataaaac gnctaaataa cacaccttta ctttttgaaa 360  
 aaaacaaaac aa 372

<210> 5  
 <211> 698  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(698)  
 <223> n = A,T,C or G

<400> 5  
 actagtanga tagaaacact gtgtcccgag agtaaggaga gaagctacta ttgattagag 60  
 cctaaccag gtttaactgca agaagaggcg ggatactttc agctttccat gtaactgtat 120  
 gcataaagcc aatgtagtcc agtttctaag atcatgttcc aagctaactg aatcccactt 180  
 caatacacac tcatgaaact ctgatggaac aataacagcg ccaagcctgt ggtatgatgt 240  
 gcacacttgc tagactcaga aaaaataacta ctctcataaa tgggtggggag tattttgggt 300  
 gacaacctac tttgcttggc tgagtgaagg aatgatattc atatnttcat ttattccatg 360  
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgcact cttgtgtata 420  
 tntccaaatn ttngtnngt cgctgcacat atctgaaatc ctatattaag antttcccaa 480  
 natgangtcc ctgggttttcc caccgcaactt gatcngtcaa ngatctcacc tctgtntgtc 540  
 ctaaaacctn ctncnngn gtttagcngg acctctcttc tcccttcccg aanaatnaag 600  
 tgtgngaaga nancnncn cccctnncn tncnncctng ccngctnnnc cncntgtngg 660

ggnggcgcgc cccgcggggg gacccccccn ttttcccc

698

<210> 6  
<211> 740  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(740)  
<223> n = A,T,C or G

<400> 6  
actagtcaaa aatgctaaaa taatttggga gaaaatattt ttttaagtagt gttatagttt 60  
catgtttatc ttttattatg tnttgtgaag ttgtgtcttt tcactaatta cctatactat 120  
gccaatattt ccttatatct atccataaca tttatactac atttgtaaga gaatatgcac 180  
gtgaaactta acactttata aggtaaaaat gaggtttcca agatttaata atctgatcaa 240  
gttcttgtaa ttcccaaata gaatggactt ggtctgttaa ggggctaagg gagaagaaga 300  
agataagggt aaaaagttgtt aatgaccaaa cattctaaaa gaaatgcaaa aaaaaattta 360  
ttttcaagcc ttcgaactat ttaaggaaaag caaaatcatt tcctanatgc atatcatttg 420  
tgagantttc tcantaatat cctgaatcat tcatttcagc tnaggcttca tgttgactcg 480  
atatgtcatc tagggaaagt ctatttcatg gtccaaacct gttgccatag ttggttaggc 540  
tttcctttaa ntgtgaanta ttnacangaa attttctctt tnanagttct tnatagggtt 600  
aggggtgtgg gaaaagcttc taacaatctg tagtgttncg tgttatctgt ncagaaccan 660  
aatnaccgat cgnangaagg actgggtcta tttacangaa cgaatnatct ngttnnntgt 720  
gtnnncaact ccngggagcc 740

<210> 7  
<211> 670  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(670)  
<223> n = A,T,C or G

<400> 7  
gctggggagc tcggcatggc ggtccccgct gcagccatgg ggccctcggc gttggggccag 60  
agcgcccccg gctcgatggc cccgtggtgc tcagtgaagc gcggcccgtc gcgctacgtg 120  
cttgggatgc aggagctgtt ccggggccac agcaagaccg cgagttcctg gcgcacagcg 180  
ccaaggtgca ctcggtggcc tggagttgcy acgggctcg cctacctcg ggtcttcgac 240  
aagacgccac gtcttcttgc tgganaanga ccgttggtca aagaaaacaa ttatcgggga 300  
catggggata gtgtggacca ctttgttggc atccaagtaa tcctgacctt tttgttacgg 360  
cgtctggaga taaaaccatt cgcactctggg atgtgaggac tacaaaatgc attgccactg 420  
tgaacactaa agggggagaa attaatatct gctggantcc tgatgggcan accattgctg 480  
tagcnacaag gatgatgtgg tgactttatt gatgccaaga aaccccgctc caaagcaaaa 540  
aaacanttcc aanttcgaag tcaccnaaat ctcttggaa aatgaacatn aatatnttct 600  
tcctgacaat ggncccttggg tgtntcacat cctcagctnc cccaaaactg aancctgtnc 660  
natccacccc 670

<210> 8  
<211> 689  
<212> DNA  
<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(689)  
 <223> n = A,T,C or G

<400> 8  
 actagtatct aggaatgaac agtaaaagag gagcagttgg ctacttgatt acaacagagt 60  
 aaatgaagta ctggatttgg gaaaacctgg ttttattaga acatatggaa tgaaagccta 120  
 cacctagcat tgcctactta gccccctgaa ttaacagagc ccaattgaga caaacccctg 180  
 gcaacaggaa attcaagga gaaaaagtaa gcaacttggg ctaggatgag ctgactccct 240  
 tagagcaaag ganagacagc ccccattacc aaataccatt tttgcctggg gcttgtgcag 300  
 ctggcagtg tctgcccc gcatggcacc ttatngtttt gatagcaact tcgttgaatt 360  
 ttcaccaact tattacttga aattataata tagcctgtcc gtttgcctgtn tccaggctgt 420  
 gatatatntt cctagtgggt tgacttttaa aataaatnag gtttantttt ctcccccn 480  
 cnntnctncc nntcnctcnn cnntcccccc cnctcngtcc tccnnnnttn gggggggcnn 540  
 cccccncggg ggacccccct ttggtccctt agtggagggt natggcccc ggnnttatcc 600  
 nggcctann tttccccgtn nnaaatgntt cccctccca ntccnccac ctcaanccgg 660  
 aagcctaagt ttntaccctg ggggtcccc 689

<210> 9  
 <211> 674  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(674)  
 <223> n = A,T,C or G

<400> 9  
 gtccactctc ctttgagtgt actgtcttac tgtgcactct gtttttcaac tttctagata 60  
 taaaaaatgc ttgttctata gtggagtaag agctcacaca cccaaggcag caagataact 120  
 gaaaaaagcg aggccttttt gccaccttgg taaaggccag ttcactgcta tagaactgct 180  
 ataagcctga aggggaagtag ctatgagact ttccattttt cttagttctc ccaataggct 240  
 ccttcatgga aaaaggcttc ctgtaataat tttcacctaa tgaattagca gtgtgattat 300  
 ttctgaaata agagacaaat tgggcccgcag agtcttctg tgatttaaaa taaacaaccc 360  
 aaagttttgt ttggtcttca ccaaaggaca tactctaggg ggtatgttgt tgaagacatt 420  
 caaaaacatt agctgttctg tctttcaatt tcaagttatt ttggagactg cctccatgtg 480  
 agttaattac tttgtctctg aactagcatt attgtcatta tcatcacatt ctgtcatcat 540  
 catctgaata atattgtgga tttccccctc tgcctgcac ttcttttgac tctctggga 600  
 anaaatgtca aaaaaaagcg tcgatctact cngcaaggnc catctaata ctgcgctgga 660  
 aggaccnct gcc 674

<210> 10  
 <211> 346  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(346)  
 <223> n = A,T,C or G

<400> 10

```

actagtctgc tgatagaaag cactatacat cctattgttt ctttctttcc aaaatcagcc      60
ttctgtctgt aacaaaaatg tactttatag agatggagga aaagggtctaa tactacatag      120
ccttaagtgt ttctgtcatt gttcaagtgt attttctgta acagaaacat atttggaatg      180
tttttctttt ccccttataa attgtaattc ctgaaatact gctgctttta aaagtcccac      240
tgtcagatta tattatctaa caattgaata ttgtaaatat acttgtctta cctctcaata      300
aaagggtact tttctattan nnagnngnnn gnnnnataaa anaaaaa      346

```

```

<210> 11
<211> 602
<212> DNA
<213> Homo sapien

```

```

<400> 11
actagtaaaa agcagcattg ccaaataatc cctaattttc cactaaaaat ataatgaaat      60
gatgttaagc tttttgaaaa gtttaggtta aacctactgt tgtagatta atgtatttgt      120
tgcttccctt tatctggaat gtggcattag cttttttatt ttaaccctct ttaattctta      180
ttcaattcca tgacttaagg ttggagagct aaacactggg atttttggat aacagactga      240
cagttttgca taattataat cggcattgta catagaaagg atatggctac cttttgttaa      300
atctgcactt tctaaatatt aaaaaaggga aatgaagtta taaatcaatt tttgtataat      360
ctgtttgaaa catgagtttt atttgcttaa tattagggct ttgccccttt tctgtaagtc      420
tcttgggata ctgtgtagaa ctgttctcat taaacaccaa acagttaagt ccattctctg      480
gtactagcta caaattcggg ttcatttctt acttaacaat ttaaataaac tgaaatatatt      540
ctagatggtc tacttctgtt catataaaaa caaaacttga tttccaaaaa aaaaaaaaaa      600
aa                                                                                   602

```

```

<210> 12
<211> 685
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(685)
<223> n = A,T,C or G

```

```

<400> 12
actagtcctg tgaagtaga actgaaggca gaaagtgtta ggattttgca tctaattgtc      60
attatcatgg tattgatgga cctaagaaaa taaaaattag actaagcccc caaataagct      120
gcatgcattt gtaacatgat tagtagattt gaatatatag atgtagtatn ttgggtatct      180
aggtgtttta tcattatgta aaggaattaa agtaaaggac tttgtagttg tttttattaa      240
atatgcatat agtagagtgc aaaaatatag caaaaatana aactaaagggt agaaaagcat      300
tttagatatg ccttaatnta nnaactgtgc caggtggccc tcggaataga tgccaggcag      360
agaccagtgc ctgggtggtg cctccccttg tctgcccccc tgaagaactt ccctcacgtg      420
angtagtgcc ctcgtaggtg tcacgtggan tantggganc aggccgnncn gtnanaagaa      480
ancanngtga nagtttcncc gtngangcng aactgtccct gngecnnnac gctcccanaa      540
cntntccaat ngacaatcga gtttcennnc tccngnaacc tngcegnnnn cnngcccnnc      600
cantntgnta accccgcgcc cggatcgctc tcnnntcggt ctncnncnaa ngggntttcn      660
cnnccgccgt cncncccccg cnncc                                                                                   685

```

```

<210> 13
<211> 694
<212> DNA
<213> Homo sapien

```

```

<220>

```

<221> misc\_feature  
 <222> (1)...(694)  
 <223> n = A,T,C or G

<400> 13  
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 agttgacgaa gatctggttt acaagaacta attaaatggt tcattgcatt tttgtaagaa 120  
 cagaataatt ttataaaatg tttgtagttt ataattgccg aaaataattt aaagacactt 180  
 tttctctgtg tgtgcaaagtg tgtgtttgtg atccattttt tttttttttt taggacacct 240  
 gtttactagc tagctttaca atatgccaaa aaaggatttc tccctgacct catccgtggt 300  
 tcacctctct tcccccccat gctttttgcc ctagtattata acaaaggaat gatgatgatt 360  
 taaaaagtag ttctgtatct tcagtatctt ggtcttccag aacctctctg ttgggaaggg 420  
 gatcattttt tactgggtcat ttcccttttg agtgactac tttaacagat ggaaagaact 480  
 cattggccat ggaaacagcc gangtggttg gagccagcag tgcattggcac cgtccggcat 540  
 ctggcgtgat tggctcggct gccgtcattg tcagcacagt gccatgggac atggggaana 600  
 ctgactgcac ngccaatggt tttcatgaag aatacngcat ncncngtgat cacgtnancc 660  
 angacgctat gggggncana gggccanttg ctcc 694

<210> 14  
 <211> 679  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(679)  
 <223> n = A,T,C or G

<400> 14  
 cagccgcctg catctgtatc cagcgccang tcccgcaggt cccagctgcg cgcgcccccc 60  
 agtcccgncac ccgttcggcc cangctnagt tagncctcac catnccggtc aaaggangca 120  
 ccaagtgcac caaataacct cngtncggat ntaaattcat cttctggctt gccgggattg 180  
 ctgtccntgc cattggacta nggctccgat ncgactctca gaccanganc atcttcganc 240  
 naganactaa tnatnattnt tccagcttct acacaggagt ctatattctg atcggatccg 300  
 gcnccctcnt gatgctggtg ggcttccctga gctgctgcgg ggctgtgcaa gagtcccant 360  
 gcatgctggg actgttcttc ggcttctctt tgggtgatn cgccattgaa atacctgcgg 420  
 ccattctggg atattccact ncgatnatgt gattaaggaa ntccacggag ttttacaagg 480  
 acacgtacaa cnacctgaaa accnnggatg anccccaccg ggaancnctg aangccatcc 540  
 actatgcgtt gaactgcaat ggtttggctg gggnccttga acaatttaac cncatacatc 600  
 tggccccann aaaggacntn ctcgannctt tcnccgtgna attcngttct gatnccatca 660  
 cagaagtctc gaacaatcc 679

<210> 15  
 <211> 695  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(695)  
 <223> n = A,T,C or G

<400> 15  
 actagtggat aaaggccagg gatgctgctc aacctcctac catgtacagg gacgtctccc 60  
 cattacaact acccaatccg aagtgtcaac tgtgtcagga ctaanaaacc ctggttttga 120

```

ttaaanaagg gcctgaaaaa aggggagcca caaatctgtc tgcttctca cnttantcnt 180
tggcaaatna gcattctgtc tcnttggtc cngcctcanc ncaaaaaanc ngaactcnat 240
cngggccagg aatacatctc ncaatnaacn aaattganca aggcnnntggg aaatgccnga 300
tgggattatc ntccgcttgt tgancttcta agtttctntc ccttcattcn accctgccag 360
ccnagttctg ttagaaaaat gccngaattc naacnccggt tttctactc ngaatttaga 420
tctncanaaa ctctctggcc acnattcnaa tt nangnca cgnacanatn ccttccatna 480
ancncacccc acntttgana gccangacaa tgactgcntn aantgaaggc ntgaaggaan 540
aactttgaaa ggaaaaaaa ctttgtttcc ggccccctcc aacncttctg tgtnnancac 600
tgcttctcng naaccctgga agcccnngga cagtgttaca tgttgttcta nnaaacngac 660
ncttnaatnt cnatcttccc nanaacgatt ncnc 695

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<210> 16

<211> 669

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (669)

<223> n = A,T,C or G

<400> 16

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cgccgaagca gcagcgagg ttgtccccgt tccccctccc ccttcccttc tccggttgcc 60
ttcccgggcc ccttacactc cacagteccg gtccccccat gtcccagaaa caagaagaag 120
agaaccctgc ggaggagacc ggcgaggaga agcaggacac gcaggagaaa gaaggtattc 180
tgcttgagag agctgaagag gcaaagctaa aggccaaaata cccaagccta ggacaaaagc 240
ctggaggctc cgacttctc atgaagagac tccagaaagg gcaaaagtac tttgactcng 300
gagactacaa catggccaaa gccaacatga agaataagca gctgccaaagt gcangaccag 360
acaagaacct ggtgactggt gatcacatcc ccaccccaca ggatctgccc agagaaagtc 420
ctcgtctgtc accagcaagc ttgggggtgg ccaagttgaa tgatgctgcc ggggctctgc 480
canatctgag acgcttccct cctgccccca cccgggtcct gtgctggctc ctgcccttcc 540
tgcttttgca gccanggggc aggaagtggc ncnggtngtg gctggaaagc aaaacccttt 600
cctgttggtg tcccacccat ggagcccctg gggcgagccc angaacttga ncctttttgt 660
tntcttnc 695

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<210> 17

<211> 697

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (697)

<223> n = A,T,C or G

<400> 17

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gcaagatatg gacaactaag tgagaaggta atnctctact gctctagntn ctcnngcnn 60
gacgcgctga ggagannnac gctggcccan ctgcccggca cacacgggga tcntggtnat 120
gctgcccann ggagncceca ncnccteggan cccatntcac acccgnncn tncgcccacn 180
ncctggetcn cncngcccng nccagctcnc gnccectcc gccnnnctcn ttnnctctc 240
cncnccctcc ncnacnacct cctaccncg gctccctccc cagccccccc ccgcaancct 300
ccacnacncc ntncnncga ancnecntc gncctcngcc cncgccccct gccccccgcc 360
cncnacnncg cgncccccg cgcncgcngc ctncccccct cccacnacag ncncacccgc 420
agncaagcnc tccgcccnet gacgcccenn cccgcgcgc tcaccttcat ggncnncng 480
ccccgetcnc ncncctgcnc gccgncnngg cgcgccgcc cncnngntn ccncnngnng 540

```

```
ccccngcngn angcngtgcg cnnccangncc gngccggnncn ncaccctccg nccncegccc 600
cgcccgctgg gggctcccg cncgcggntc antcccncc cntnccccca ctntccgntc 660
cnnnctcnc gctcngcgn cgcncncnc cccccc 697
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<210> 18

<211> 670

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(670)

<223> n = A,T,C or G

<400> 18

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ctcgtgtgaa ggggtgcagta cctaagccgg agcggggtag aggcgggccc gcacccccctt 60
ctgacctcca gtgccgccc cctcaagatc agacatggcc cagaacttga acgacttggc 120
gggacggctg cccgccgggc cccggggcat gggcacggcc ctgaagctgt tgctgggggc 180
cggcgccgtg gcctacgggtg tgcgcgaatc tgtgttcacc gtggaaggcg ggcncagagc 240
catcttcttc aatcggatcg gtggagtga caggacacta tcctgggccc anggccttca 300
cttcaggatc cttggttcca gtaccccanc atctatgaca ttcgggccag acctcgaaaa 360
aatctcctcc ctacaggctc caaagacctc cagatggtga atatctccct gcgagtgttg 420
tctcgaccaa tgctcangaa cttcctaaca tgttccancg cctaagggct ggactacnaa 480
gaacgantgt tgccgtccat tgtcacgaag tgctcaagaa tttnggtggc caagttcaat 540
gncctcacnn ctgatcnccc agcggggcca agttanccct ggttgatccc cgggganctg 600
acnnaaaagg gccaaaggact tcccctcatc ctggataatg tggcctcac aaagctcaac 660
tttanccacc 670
```

<210> 19

<211> 606

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(606)

<223> n = A,T,C or G

<400> 19

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actagtgcc aacctcagctc ccaggccagt tctctgaatg tcgaggagtt ccaggatctc 60
tggcctcagt tgtccttggg tattgatggg ggacaaattg gggatggcca gagccccgag 120
tgtcgcttg gctcaactgt ggttgatttg tctgtgccc gaaagtttg catcattcgt 180
ccaggctgtg ccttgaaaag tactacagcc atcctccaac agaagtacgg actgctcccc 240
tcacatgcgt cctacctgtg aaactctggg aagcaggaag gcccaagacc tgggtgctga 300
tactatgtgt ctgtccactg acgactgtca aggcctcatt tgcagaggcc accggagcta 360
gggcactagc ctgactttta aggcagtgtg tctttctgag cactgtagac caagcccttg 420
gagctgctgg tttagccttg cacttgggga aaggatgtat ttatttgtat tttcatatat 480
cagccaaaag ctgaatggaa aagttnagaa cattcctagg tggccttatt ctaataagtt 540
tcttctgtct gttttgtttt tcaattgaaa agttattaaa taacagattt agaattcagt 600
gagacc 606
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<210> 20

<211> 449

<212> DNA

<213> Homo sapien



&lt;400&gt; 20

actagtaa	aacagcag	ca gaaacatcag	tatcagcagc	gtcgcagca	ggagaatatg	60
cagcgccaga	gccgaggaga	acccccgctc	cctgaggagg	acctgtccaa	actcttcaaa	120
ccaccacagc	cgctgccag	gatggactcg	ctgctcattg	caggccagat	aaacacttac	180
tgccagaaca	tcaaggagtt	cactgccc	aaacttaggca	agctcttcat	ggcccaggct	240
cttcaagaat	acaacaacta	agaaaaggaa	gtttccagaa	aagaagttaa	catgaactct	300
tgaagtcaca	ccagggcaac	tcttggaaga	aatatatttg	catattgaaa	agcacagagg	360
atttcttttag	tgtcattgcc	gattttggct	ataacagtgt	ctttctagcc	ataataaaat	420
aaaacaaaat	cttgactgct	tgctcaaaa				449

&lt;210&gt; 21

&lt;211&gt; 409

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 21

tatcaatcaa	ctgggtgaata	attaaacaat	gtgtggtgtg	atcatataaaa	gggtaccact	60
caatgataaa	aggaacaagc	tgcctatatg	tggaacaaca	tggatgcatt	tcagaaaactt	120
tatgtttgagt	gaaagaacaa	acacggagaa	catactatgt	ggttctcttt	atgtaacatt	180
acagaaataa	aaacagaggc	aaccaccttt	gaggcagtat	ggagtggat	agactggaaa	240
aaggaaggaa	ggaaactcta	cgctgatgga	aatgtctgtg	tcttcattgg	gtggtagtta	300
tgtggggata	tacatttgtc	aaaatttatt	gaactatata	ctaaagaact	ctgcatttta	360
ttgggatgta	aataatacct	caattaaaaa	gacaaaaaaa	aaaaaaaaaa		409

&lt;210&gt; 22

&lt;211&gt; 649

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(649)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 22

acaattttca	ttatcttaag	cacattgtac	atttctacag	aacctgtgat	tattctcgca	60
tgataaggat	ggtacttgca	tatggtgaat	tactactgtt	gacagtttcc	gcagaaatcc	120
tatttcagtg	gaccaacatt	gtggcatggc	agcaaatgcc	aacattttgt	ggaatagcag	180
caaatctaca	agagaccctg	gttggttttt	cgttttgttt	tctttgtttt	ttcccccttc	240
tcctgaatca	gcagggatgg	aangagggtg	gggaagttaa	gaattactcc	ttccagtagt	300
agctctgaag	tgtcacattt	aatatcagtt	ttttttaaac	atgattctag	ttnaatgtag	360
aagagagaag	aaagaggaag	tgttcacttt	tttaatacac	tgatttagaa	atttgatgtc	420
ttatatcagt	agttctgagg	tattgatagc	ttgctttatt	tctgccttta	cgttgacagt	480
gttgaagcag	ggtgaataac	taggggcata	tatatTTTTT	TTTTTTgtaa	gctgtttcat	540
gatgttttct	ttggaatttc	cggataagtt	caggaaaaca	tctgcatggt	gttatctagt	600
ctgaagtten	tatccatctc	attacaacaa	aaacnccag	aacggnnttg		649

&lt;210&gt; 23

&lt;211&gt; 669

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(669)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 23

actagtgccg	tactggctga	aatccctgca	ggaccaggaa	gagaaccagt	tcagactttg	60
tactctcagt	caccagctct	ggaattagat	aaattccttg	aagatgtcag	gaatgggata	120
tatcctctga	cagcctttgg	gctgcctcgg	ccccagcagc	cacagcagga	ggaggtgaca	180
tcacctgtcg	tgcccccttc	tgtcaagact	ccgacacctg	aaccagctga	ggtggagact	240
cgcaagggtg	tgctgatgca	gtgcaacatt	gagtcgggtg	aggagggagt	caaacaccac	300
ctgacacttc	tgctgaagtt	ggaggacaaa	ctgaaccggc	acctgagctg	tgacctgatg	360
ccaaatgaga	atatccccga	gttggcggct	gagctgggtg	agctgggctt	cattagttag	420
gctgaccaga	gccggttgac	ttctctgcta	gaagagactt	gaacaagttc	aattttgcca	480
ggaacagtac	cctcaactca	gccgctgtca	ccgtctcctc	ttagagctca	ctcgggccag	540
gccctgatct	gcgctgtggc	tgtcctggac	gtgctgcacc	ctctgtcctt	ccccccagtc	600
agtattacct	gtgaagccct	tccctccttt	attattcagg	anggetgggg	gggctccttg	660
nttctaacc						669

&lt;210&gt; 24

&lt;211&gt; 442

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 24

actagtacca	tcttgacaga	ggatacatgc	tcccaaaacg	tttgttacca	cacttaaaaa	60
tcactgccat	cattaagcat	cagtttcaaa	attatagcca	ttcatgattt	actttttcca	120
gatgactatc	attattctag	tcctttgaat	ttgtaagggg	aaaaaaaaa	aaaacaaaaa	180
cttacgatgc	acttttctcc	agcacatcag	atttcaaatt	gaaaattaaa	gacatgctat	240
ggtaatgcac	ttgctagtac	tacacacttt	ggtacaacaa	aaaacagagg	caagaaacaa	300
cggaagagag	aaagccttcc	tttgttggcc	cttaaaactga	gtcaagatct	gaaatgtaga	360
gatgatctct	gacgatacct	gtatgttctt	attgtgtaaa	taaaattgct	ggtatgaaat	420
gacctaaaaa	aaaaaaaaa	aa				442

&lt;210&gt; 25

&lt;211&gt; 656

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(656)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 25

tgcaagtacc	acacactgtt	tgaattttgc	acaaaaagtg	actgtaggat	caggatgatag	60
ccccggaatg	tacagtgtct	tggtgcacca	agatgccttc	taaaggctga	cataccttgg	120
accctaattg	ggcagagagt	atagccctag	cccagtgggtg	acatgaccac	tccttttggg	180
aggcctgagg	tagaggggag	tggtatgtgt	tttctcagtg	gaagcagcac	atgagtgggt	240
gacaggatgt	tagataaagg	ctctagttag	gggtgcattg	tcatttgaga	gactgacaca	300
ctcctagcag	ctggtaaagg	gggtgctggan	gccatggagg	anctctagaa	acattagcat	360
gggctgatct	gattacttcc	tggtatcccc	ctcactttta	tggaagtctt	tattagangg	420
atgggacagt	tttccatata	cttgcgtgtg	agctctggaa	cactctctaa	atttccctct	480
attaaaaatc	actgccctaa	ctacacttcc	tccttgaaag	aatagaatg	gaactttctc	540
tgacatantt	cttggcatgg	ggagccagcc	acaaatgana	atctgaacgt	gtccagggtt	600
ctcctganac	tcattctacat	agaattgggt	aaacctcccc	ttggaataag	gaaaaa	656

<210> 26  
 <211> 434  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(434)  
 <223> n = A,T,C or G

<400> 26  
 actagttcag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60  
 ctagggtgtt ccatctatgt ttcaatctgt ccatctacca ggcctcgcga taaaaacaaa 120  
 acaaaaaaac gctgccagggt tttagaagca gttctgggtct caaaaccatc aggatcctgc 180  
 caccagggtt cttttgaaat agtaccacat gtaaaagggga atttggtttt cacttcatct 240  
 aataactgaa ttgtcagggt ttgattgata attgtagaaa taagtagcct tctgttgttg 300  
 gaataagtta taatcagtat tcactctctt gttttttgtc actcttttct ctctaattgt 360  
 gtcatttgta ctggttgaaa aatatttctt ctatnaaatt aaactaacct gccttaaaaa 420  
 aaaaaaaaaa aaaa 434

<210> 27  
 <211> 654  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(654)  
 <223> n = A,T,C or G

<400> 27  
 actagtccaa cacagtcaga aacattgttt tgaatcctct gtaaaccaag gcattaatct 60  
 taataaacca ggatccattt aggtaccact tgatataaaa aggatatcca taatgaatat 120  
 tttatactgc atcctttaca ttagccacta aatacggttat tgcttgatga agacctttca 180  
 cagaatccta tggattgcag catttcactt ggctacttca taccatgcc ttaaagaggg 240  
 gcagtttctc aaaagcagaa acatgccgcc agttctcaag ttttcctctt aactccattt 300  
 gaatgtaagg gcagctggcc cccaatgttg ggaggtccga acattttctg aattcccatt 360  
 ttcttgttcg cggctaaatg acagtttctg tcattactta gattccgac tttcccaaag 420  
 gtgttgattt acaaagaggc cagctaatag cagaaatcat gaccctgaaa gagagatgaa 480  
 attcaagctg tgagccaggc agganctcag tatggcaaag gtcttgagaa tcngccattt 540  
 ggtacaaaaa aaatttttaa gcntttatgt tataccatgg aaccatagaa anggcaaggg 600  
 aattgttaag aanaatttta agtgccaga ccanaanga aaaaaaaaaa aaaa 654

<210> 28  
 <211> 670  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(670)  
 <223> n = A,T,C or G

<400> 28  
 cgtgtgcaca tactgggagg atttccacag ctgcacgggtc acagccctta cggattgcc 60

```

ggaaggggag aaagatatgt gggataaact gagaaaagaa nccaaaaacc tcaacatcca 120
aggcagctta ttcgaactct gcggcagcgg caacggggcg gcgggggtccc tgctcccggc 180
gttcccgggtg ctctctgggtg ctctctcggc agcttttagcg acctgncttt ccttctgagc 240
gtggggccag ctccccccgc ggcgcccacc cacnctcact ccatgctccc ggaaatcgag 300
aggaagatca ttagttcttt ggggacgttn gtgattctct gtgatgctga aaaacactca 360
tatagggaat gtgggaaatc ctganctctt tnttatntcg tntgatttct tgtgttttat 420
ttgccaaaat gttaccaatc agtgaccaac cnagcacagc caaaaatcgg acntcngctt 480
tagtccgtct tcacacacag aataagaaaa cggcaaaccc accccacttt tnantttnat 540
tattactaan ttttttctgt tgggcaaaaag aatctcagga acngccctgg ggccnccgta 600
ctanagttaa ccnagctagt tncatgaaaa atgatgggct ccnctcaat gggaagcca 660
agaaaaagnc 670

```

```

<210> 29
<211> 551
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(551)
<223> n = A,T,C or G

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```

<400> 29
actagtcctc cacagcctgt gaatccccct agacctttca agcatagtga gcggagaaga 60
agatctcagc gtttagccac cttacccatg cctgatgatt ctgtagaaaa ggtttcttct 120
ccctctccag ccactgatgg gaaagtattc tccatcagtt ctcaaaatca gcaagaatct 180
tcagtaccag aggtgcctga tgttgacatc ttgccacttg agaagctggg accctgtctc 240
cctcttgact taagtctggg ttcagaagtt acagcaccgg tagcctcaga ttcctcttac 300
cgtaataaat gtcccagggc agaaaaagag gatacnaga tgcttccaaa tccttcttcc 360
aaagcaatag ctgatgggaa gaggagctcc agcagcagca ggaatatcga aaacagaaaa 420
aaaagtgaag ttgggaaagc aaaagctcaa cagcatttgg taaggagaaa aganaagatg 480
aggaagggaag agagaagaga gacnaagatc nctacggacc gnnncggaag aagaagaagn 540
aaaaaanaaa a 551

```

```

<210> 30
<211> 684
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(684)
<223> n = A,T,C or G

```

```

<400> 30
actagttcta tctggaaaaa gcccggttg gaagaagctg tggagagtgc gtgtgcaatg 60
cgagactcat ttcttggaag catccctggc aaaaatgcag ctgagtacaa gggtatcact 120
gtgatagaac ctggactgct ttttgagata atagagatgc tgcagtctga agagacttcc 180
agcacctctc agttgaatga attaagtatg gcttctgagt caactttact ggctcaggaa 240
ccacgagaga tgactgcaga tgtaatcgag cttaaaggga aattcctcat caacttagaa 300
gggtggtgata ttcgtgaaga gtcttcctat aaagtaattg tcatgccgac tacgaaagaa 360
aaatgcccc gttgttgga gatacagcg ggagtcttca gataactgt gtcctcgatg 420
tgcagaagtt gtcagtggga aaatagtatt aacagctcac tcgagcaaga accctcctga 480
cagtactggg ctagaagttt ggatggatta tttacaatat aggaaagaaa gccagaat 540
aggtnatgag tggatgagta aatggtggan gatggggaat tcaaatacga attatggaag 600

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aagtntttcc tgttactata gaaaggaatt atgtttatatt acatgcagaa aatatanatg 660  
 tgtggtgtgt accgtggatg gaan 684

<210> 31  
 <211> 654  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(654)  
 <223> n = A,T,C or G

<400> 31  
 gcgcagaaaa ggaaccaata tttcagaaac aagcttaata ggaacagctg cctgtacatc 60  
 aacatcttct cagaatgacc cagaagttat catcgtggga gctggcgtgc ttggctctgc 120  
 tttggcagct gtgctttcca gagatggaag aaagggtgaca gtcattgaga gagacttaaa 180  
 agagcctgac agaatagttg gagaattcct gcagccgggt ggttatcatg ttctcaaaga 240  
 ccttggtctt ggagatacag tggaaaggtct tgatgccag gttgtaaattg gttacatgat 300  
 tcatgatcag ggaaagcaaa tcagangttc agattcctta ccctctgtca gaaaacaatc 360  
 aagtgcagag tggaaagagct ttccatcacg gaagattcat catgagtctc cggaaagcag 420  
 ctatggcaga gcccaatgca aagtttattg aagggtgtgt gttacagtta ttagaggaag 480  
 atgatgttgt gatgggagtt cagtacaagg ataaagagac tgggagatat caaggaactc 540  
 catgctccac tgactgttgt tgcagatggg cttttctcca anttcaggaa aagcctggtc 600  
 tcaataaagt ttctgtatca ctcatttggt tggtctctta tgaagaatgc nccc 654

<210> 32  
 <211> 673  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(673)  
 <223> n = A,T,C or G

<400> 32  
 actagtgaag aaaaagaaat tctgatacgg gacaaaaatg ctcttcaaaa catcattctt 60  
 tatcacctga caccaggagt tttcattgga aaaggatttg aacctgggtg tactaacatt 120  
 ttaaagacca cacaaggaag caaaatcttt ctgaaagaag taaatgatac acttctgggtg 180  
 aatgaattga aatcaaaaaga atctgacatc atgacaacaa atgggtgtaat tcatgttgta 240  
 gataaaactcc tctatccagc agacacacct gttggaaatg atcaactgct ggaaatactt 300  
 aataaattaa tcaaatatcat ccaaatttaag tttgttcgtg gtagcacctt caaagaaatc 360  
 cccgtgactg tctatnagcc aattattaaa aaatacacca aaatcattga tgggagtgcc 420  
 tgtgggaaat aactgaaaaa gagaccgaga agaacgaatc attacaggtc ctgaaataaa 480  
 atacctagga tttctactgg aggtggagaa acagaagaac tctgaagaaa ttgttacaag 540  
 aagangtccc aaggtcacca aattcattga aggtgggtgat ggtctttatt tgaagatgaa 600  
 gaaattaaaa gacgcttcag ggagacnccc catgaaggaa ttgccagcca caaaaaaatt 660  
 cagggattag aaa 673

<210> 33  
 <211> 673  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(673)  
 <223> n = A,T,C or G

<400> 33  
 actagttatt tactttcctc cgcttcagaa ggtttttcag actgagagcc taagcatact 60  
 ggatctgttg tttcttttgg gtctcacctc atcagtgtgc atagtggcag aaattataaa 120  
 gaaggttgaa aggagcaggg aaaagatcca gaagcatgtt agttcgacat catcatcttt 180  
 tcttgaagta tgatgcatat tgcattattt tatttgcaaa ctaggaattg cagtctgagg 240  
 atcatttaga agggcaagtt caagaggata tgaagatttg agaacttttt aactattcat 300  
 tgactaaaaa tgaacattaa tgttnaagac ttaagacttt aacctgctgg cagtcccaaa 360  
 tgaaattatg caactttgat atcatattcc ttgatttaaa ttgggctttt gtgattgant 420  
 gaaactttat aaagcatatg gtcagttatt tnattaaaaa ggcaaaacct gaaccacctt 480  
 ctgcacttaa agaagtctaa cagtacaaat acctatctat cttagatgga tntatttntt 540  
 tntattttta aatattgtac tatttatggg nggtggggct ttcttactaa tacacaaatn 600  
 aatttatcat ttcaanggca ttctatttgg gtttagaagt tgattccaag nantgcatat 660  
 ttcgctactg tnt 673

<210> 34  
 <211> 684  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(684)  
 <223> n = A,T,C or G

<400> 34  
 actagtttat tcaagaaaag aacttactga ttctctgtt cctaaagcaa gagtggcagg 60  
 tgatcagggc tgggtgtagca tccggttcct ttagtgagc taactgcatt tgtcactgat 120  
 gaccaaggag gaaatcacta agacatttga gaagcagtg tatgaacgtt cttggacaag 180  
 ccacagttct gagcettaac cctgtagttt gcacacaaga acgagctcca cctccccttc 240  
 ttcaggagga atctgtgcgg atagattggc tggacttttc aatggttctg ggttgcaagt 300  
 gggcactgtt atggctgggt atggagcggc cagccccagg aatcagagcc tcagcccggc 360  
 tgcctggttg gaaggtacag gtgttcagca ccttcggaaa aagggcataa agtngtgggg 420  
 gacaattctc agtccaagaa gaatgcattg accattgctg gctatttgct tncctagtat 480  
 gaattggatn catttttgac cangatnntt ctncatgct tnttgcaat gaaatcaaat 540  
 cccgcattat ctacaagtgg tatgaagtcc tgcnncccc agagaggctg ttcaggcnat 600  
 gtcttccaag ggcagggtgg gttacaccat ttacctccc ctctcccccc agattatgna 660  
 cncagaagga atttntttcc tccc 684

<210> 35  
 <211> 614  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(614)  
 <223> n = A,T,C or G

<400> 35  
 actagtccaa cgcgttingcn aatattcccc tggtagccta cttccttacc cccgaatatt 60

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ggtaagatcg agcaatggct tcaggacatg ggttctcttc tctgtgacg attcaagtgc 120
tcaactgcatg aagactggct tgtctcagtg tntcaacctc accagggctg tctcttggtc 180
cacacctcgc tccctgttag tgccgtatga cagcccccat canatgacct tggccaagtc 240
acggtttctc tgtgtgcaat gttggtnggc tgattgggtg aaagtanggt ggaccaaagg 300
aagncncgtg agcagncanc nccagttctg caccagcagc gcctccgtcc tactnggggtg 360
ttcngtttc tcttggccct gngtgggcta nggcttgatt cggaanatt cctttgcang 420
gaaggganga taantgggat ctaccaattg attctggcaa aacnatntct aagattnttn 480
tgctttatgt ggganacana tctanctctc atttntgtct gnanatnaca cctactcgt 540
gntcgancnc gtcttcgatt ttcgganaca cncantnaa tactggcggt ctgttggtta 600
aaaaaaaaa aaaa 614

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<210> 36

<211> 686

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(686)

<223> n = A,T,C or G

<400> 36

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gtggctggcc cggttctcgc cttctcccca tcccctactt tctccctcc ctcctttcc 60
ctccctcgtc gactgttgct tgctggtcgc agactccctg acccctccct caccctccc 120
taacctcggg gccaccggat tgcccttctt ttctgttgcc ccagcccagc cctagtgtca 180
gggcgggggc ctggagcagc ccgaggcact gcagcagaag ananaaaaga cagcacnaac 240
ctcagctcgc cagtcgggtc gctngcttcc cgccgcatgg caatnagaca gacgcgcctc 300
acctgctctg ggcacacgcg acccgtggtt gatttggcct tcagtggcat cacccttatg 360
ggtatttctt aatcagcgcg tgcaaagatg gttaacctat gctacgccag ggagatacag 420
gagactggat tggaacattt ttgggttcta aaggctctgt tggggtgcaa cactgaataa 480
ggatgccacc aaagcagcta cagcagctgc agatttcaca gccaagtgt gggatgctgt 540
ctcagganat naattgataa cctggctcat aacacattgt caagaatgtg gatttcccca 600
ggatattatt atttgtttac cggggganag gataactgtt tcncntattt taattgaaca 660
aactnaaaca aanctaagg aaatcc 686

```

<210> 37

<211> 681

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(681)

<223> n = A,T,C or G

<400> 37

```

gagacanacn naagtcang agaanaaaag angcatggaa cacaanccag gcncgatggc 60
caccttccca ccagcancca gcgccccca gcngccccca ngncggang accangactc 120
cancctgnat caatctganc tctattcctg gcccatnccct acctcggagg tggangccgn 180
aaaggtcgca cnnncagaga agctgctgcc ancaccance gcccnnccc tgnccggctn 240
nataggaaac tggtgaccnn gctgcanaat tcatacagga gcacgchang ggacnncct 300
cacactgagt tnnngatgan gcctnaccan ggacctnccc cagcnnattg annacnggac 360
tgccggaggaa ggaagacccc gnacnggatc ctggccggcn tgccaccccc ccaccctag 420
gattatnccc cttgactgag tctctgaggg gctacccgaa cccgcctcca ttccctacca 480
natntgtctc natcgggact gacangctgg ggatnggagg ggctatcccc cancatcccc 540

```

tnanaccaac agcnacngan natngggggt cccnngggtc ggngcaacnc tectncaccc 600  
cggcgcnggc cttegggtgnt gtctctcentc aacnaattcc naaanggcgg gccccccngt 660  
ggactcctcn ttgttcctc c 681

<210> 38

<211> 687

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(687)

<223> n = A,T,C or G

<400> 38

canaaaaaaaa aaaacatggc cgaaaccagn aagctgcgcg atggcgccac ggccccctctt 60  
ctcccgccct gtgtccggaa ggtttcctc cgaggcgccc cggctcccg aagcggagga 120  
gagggcggga cntgcgggg cggagctca naggccctgg ggccgctctg ctctcccgcc 180  
atcgcaagg cggcgctaac ctnaggcctc cccgcaaagg tccccnangc ggnggcggcg 240  
gggggctgtg anaaccgcaa aaanaacgct gggcgcgeng cgaaccgctc ccccccgcg 300  
aaggananac ttccacagan gcagcgtttc cacagccan agccacnttt ctagggtgat 360  
gcacccagc aagttcctgn cggggaagct caccgctgtc aaaaaanctc ttcgctccac 420  
cggcgcacna agggangan ggcanangc tgccgcccgc acaggtcatc tgatcacgtc 480  
gcccgcctta ntctgctttt gtgaatctcc actttgttca accccaccgc cgttctctc 540  
ctccttgccg ctctctctna ccttaanaac cagcttctc taccnctng tanttctct 600  
gcncnngtng aaattaatc ggtccnccgg aacctcttnc ctgtggcaac tgctnaaaga 660  
aactgctgtt ctgnttactg cngtccc 687

<210> 39

<211> 695

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(695)

<223> n = A,T,C or G

<400> 39

actagtctgg cctacaatag tgtgattcat gtaggacttc tttcatcaat tcaaaacccc 60  
tagaaaaacg tatacagatt atataagtag ggataagatt tctaacattt ctgggctctc 120  
tgacccctgc gctagactgt ggaaaggag tattattata gtatacaaca ctgctgttgc 180  
cttattagtt ataacatgat aggtgctgaa ttgtgattca caatttaaaa aactgtaat 240  
ccaaactttt ttttttaact gtagatcatg catgtgaatg ttaatgttaa tttgttcaan 300  
gttggttatgg gtagaaaaaa ccacatgcct taaaatttta aaaagcaggg cccaaactta 360  
ttagtttaaa attaggggta tgtttccagt ttgttattaa ntgggtatag ctctgtttag 420  
aanaaatcna ngaacangat ttngaaantt aagntgacat tatttnccag tgacttgta 480  
atttgaaatc anacacggca ccttcggtt ttgtnctatt ggnntttgaa tccaancng 540  
ntccaaatct tnttggaac ngtcnctta actttttac nanatcttat tttttattt 600  
tggaatggcc ctatttaang ttaaaagggg ggggnccac naccattcnt gaataaaact 660  
naatatatat ccttggtccc ccaaaattta agng 695

<210> 40

<211> 674

<212> DNA



<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(674)

<223> n = A,T,C or G

<400> 40

actagtagtc agttgggagtg ggttgctata ccttgacttc atttatatga atttccactt	60
tattaaataa tagaaaaagaa aatcccgggtg cttgcagtag agttatagga cattctatgc	120
ttacagaaaa tatagccatg attgaaatca aatagtaaag gctgttctgg ctttttatct	180
tcttagctca tcttaaataa gtagtacact tgggatgcag tgcgtctgaa gtgctaataca	240
gttgtaacaa tagcacaaat cgaacttagg atgtgtttct tctcttctgt gtttcgattt	300
tgatcaattc ttttaattttg ggaacctata atacagtttt cctattcttg gagataaaaa	360
ttaaatggat cactgatatt taagtcattc tgcttctcat ctnaatattc catattctgt	420
attagganaa antacctccc agcacagccc cctctcaaac cccacccaaa accaagcatt	480
tggaatgagt ctctcttatt tccgaantgt ggatgggtata acccatatcn ctccaatttc	540
tgnttgggtt ggggtattaat ttgaactgtg catgaaaagn ggnaatcttt nctttgggtc	600
aaantttncg ggttaatttg nctngncaaa tccaatttnc ttttaagggtg tctttataaa	660
atttgctatt cngg	674

<210> 41

<211> 657

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(657)

<223> n = A,T,C or G

<400> 41

gaaacatgca agtaccacac actgtttgaa ttttgcacaa aaagtgactg tagggatcag	60
gtgatagccc cggaatgtac agtgtcttg tgcaccaaga tgccttctaa aggctgacat	120
accttgggac cctaattggg cagagagtat agccctagcc cagtggtgac atgaccactc	180
cctttgggag gctgaagtta aaggggaatgg tatgtgtttt ctcatggaag cagcacatga	240
atnggtnaca ngatgttaaa ntaaggntct antttgggtg tcttgtcatt tgaaaaantg	300
acacactcct ancanctggg aaaggggtgc tggaagccat ggaagaactc taaaaacatt	360
agcatgggct gatctgatta ctccctggca tcccgtcac ttttatggga agtcttatta	420
naaggatggg ananttttcc atatccttgc tgttggaact ctggaacact ctctaaattt	480
ccctctatta aaaatcactg nccttactac acttctcct tganggaata gaaatggacc	540
tttctctgac ttagttcttg gcatggganc cagcccaaat taaaatctga cttntccggt	600
ttctccngaa ctacactact tgaattggtg aaacctcctt tggaattagn aaaaacc	657

<210> 42

<211> 389

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(389)

<223> n = A,T,C or G

<400> 42

```

actagtgcctg aggaatgtaa acaagtttgc tgggccttgc gagacttcac caggttggtt 60
cgatagctca cactcctgca ctgtgcctgt caccacaggaa tgtctttttt aattagaaga 120
caggaagaaa acaaaaacca gactgtgtcc cacaatcaga aacctccgtt gtggcagang 180
ggccttcacc gccaccaggg tgtcccgcca gacagggaga gactccagcc ttctgaggcc 240
atcctgaaga attcctgttt ggggggttgtg aaggaaaatc acccggattt aaaaagatgc 300
tgttgcctgc ccgcgtngtn gggaaggac tggtttcctg gtgaatttct taaaagaaaa 360
atattttaag ttaagaaaaa aaaaaaaaaa 389

```

&lt;210&gt; 43

&lt;211&gt; 279

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 43

```

actagtgcac agtcctgggt cttgagatgt cttctcggtta aggagatggg ccttttggtg 60
gtaaaggata aaatgaatga gttctgtcat gattcactat tctagaactt gcatgacctt 120
tactgtgtta gctctttgaa tgttcttgaa atttttagact ttctttgtaa acaataata 180
tgctcttacc attgtataaa agctgttatg tgcaacagtg tggagatcct tgtctgattt 240
aataaaatac ttaaactctg aaaaaaaaaa aaaaaaaaaa 279

```

&lt;210&gt; 44

&lt;211&gt; 449

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(449)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 44

```

actagtagca tcttttctar aacgttaaaa ttgcagaagt agcttatcat taaaaaacia 60
caacaacaac aataacaata aatcctaagt gtaaatcagt tattctaccc cctaccaagg 120
atatcagcct gttttttccc ttttttctcc tgggaataat tgtgggcttc ttcccaaatt 180
tctacagcct ctttctctct ctcagtcttg agcttccttg tttgcacgca tgcgttggtc 240
aagantgggc tgtttngctt ggantnecgt ccnagtggaa ncatgcttcc ccttggtact 300
gttggaagaa actcaaacct tcnancccta ggtgttncca ttttgtaag tcatcactgt 360
atttttgtac tggcattaac aaaaaaagaa atnaaatatt gttccattaa actttaataa 420
aactttaaaa gggaaaaaaa aaaaaaaaaa 449

```

&lt;210&gt; 45

&lt;211&gt; 559

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(559)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 45

```

actagtgtgg gggaatcacg gacacttaaa gtcaatctgc gaaataattc ttttattaca 60
cactcactga agtttttgag tcccagagag ccattctatg tcaaacattc caagtactct 120
ttgagagccc agcattacat caacatgccc gtgcagttca aaccgaagtc cgcaggcaaa 180
tttgaagctt tgcttgatcat tcaaacagat gaaggcaaga gtattgctat tcgactaatt 240

```

```

ggtagaagctc ttggaaaaaa ttnactagaa tactttttgt gttaagttaa ttacataagt    300
tgtattttgt taactttatc tttctacact acaattatgc ttttgatat atattttgta    360
tgatggatat ctataattgt agattttgtt tttaacaagct aatactgaag actcgactga    420
aatattatgt atctagccca tagtattgta ctttaactttt acagggtgaa aaaaaaatc    480
tgtgtttgca ttgattatga tattctgaat aaatatggga atatatttta atgtgggtaa    540
aaaaaaaaaa aaaaaggaa                                     559

```

```

<210> 46
<211> 731
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G

```

```

<400> 46
actagttcta gtaccatggc tgtcatagat gcaaccatta tattccattt agtttcttcc    60
tcaggttccc taacaattgt ttgaaactga atatatatgt ttatgtatgt gtgtgtgttc    120
actgtcatgt atatggtgta tatgggatgt gtgcagtttt cagttatata tatattcata    180
tatacatatg catatatatg tataatatac atatatacat gcatacactt gtataatata    240
catatatata cacatatatg cacacatatn atcactgagt tccaaagtga gtctttattt    300
ggggcaattg tattctctcc ctctgtctgc tctctgggcc ttgcaagac atagcaattg    360
cttgatttcc tttggataag agtcttatct tgggcactct tgactctagc cttaacttta    420
gatttctatt ccagaatacc tctcatatct atcttaaaac ctaaganggg taaagangtc    480
ataagattgt agtatgaaag antttgctta gttaaattat atctcaggaa actcattcat    540
ctacaaatta aattgtaaaa tgatggtttg ttgtatctga aaaaatgttt agaacaagaa    600
atgtaactgg gtacctgtta tatcaaagaa cctcnattta ttaagtctcc tcatagccan    660
atccttatat ngccctctct gacctgantt aatananact tgaataatga atagttaatt    720
taggnntggg c                                     731

```

```

<210> 47
<211> 640
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(640)
<223> n = A,T,C or G

```

```

<400> 47
tgcgngccgg tttggccctt ctttgtanga cactttcacc cgccctgaaa tcttcccgat    60
cgtaataaac tcctcaggte cctgcctgca cagggttttt tcttantttg ttgcctaaca    120
gtacaccaa tgtgacatcc tttcaccaat atngattnct tcataccaca tcntcnatgg    180
anacgactnc aacaattttt tgatnaccn aaanactggg ggctnnaana agtacantct    240
ggagcagcat ggacctgtcn gcnactaang gaacaanagt nntgaacatt tacacaacct    300
ttggtatgtc ttactgaaa anagaaacat gcttctnncc ctagaccacg aggncaaccg    360
caganattgc caatgccaa tccgagcggt tagatcagg taaacattcc atggatgcat    420
tacatacntt gtccccgaaa nanaagatgc cctaanggct tcttcnact ggccngaaa    480
acanctacac ctgggtgctg ganaacanac tctttggaag atcatctggc acaagttccc    540
cccagtggtt tttnccttgg cacctanctt accanactna ttcggaancc attctttgcc    600
ntggcnttnt nttgggacca ntcttctcac aactgnaccc                                     640

```

<210> 48  
 <211> 257  
 <212> DNA  
 <213> Homo sapien

<400> 48  
 actagtatat gaaaatgtaa atatcacttg tgtactcaaa caaaagttgg tcttaagctt 60  
 ccaccttgag cagccttgga aacctaacct gcctctttta gcataatcac attttctaaa 120  
 tgattttctt tgttcctgaa aaagtgattt gtattagttt tacatttggt ttttggaaga 180  
 ttatatattgt atatgtatca tcataaaata tttaaataaa aagtatcttt agagtgaaaa 240  
 aaaaaaaaaa aaaaaaa 257

<210> 49  
 <211> 652  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (652)  
 <223> n = A,T,C or G

<400> 49  
 actagttcag atgagtggtt gctgaagggg ccccttctgc attttcatta taacccaatt 60  
 tccacttatt tgaactctta agtcataaat gtataatgac ttatgaatta gcacagttaa 120  
 gttgacacta gaaactgccc atttctgtat tacactatca aataggaaac attggaaaga 180  
 tggggaaaaa aatcttattt taaaatggct tagaaagttt tcagattact ttgaaaattc 240  
 taaacttctt tctgtttcca aaacttgaaa atatgtagat ggactcatgc attaagactg 300  
 ttttcaaagc tttcctcaca tttttaaaagt gtgattttcc ttttaataata catatttatt 360  
 ttctttaaag cagcttatat ccaacccatg actttggaga tataacctatn aaaccaatat 420  
 aacagcangg ttattgaagc agcttttctca aatgttgctt cagatgtgca agttgcaaat 480  
 tttattgtat ttgtanaata caatttttgt tttaaactgt atttcaatct atttctccaa 540  
 gatgcttttc atatagagtg aaatatccca ngataactgc ttctgtgtcg tcgcatttga 600  
 cgcataactg cacaaatgaa cagtgtatac ctcttggttg tgcattnacc cc 652

<210> 50  
 <211> 650  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (650)  
 <223> n = A,T,C or G

<400> 50  
 ttgcgctttg attttttttag ggcttgtgcc ctgtttcact tatagggtct agaatgcttg 60  
 tgttgagtaa aaaggagatg cccaatatcc aaagctgcta aatgttctct ttgccataaa 120  
 gactccgtgt aactgtgtga acacttgga tttttctcct ctgtcccgag gtcgtcgtct 180  
 gctttctttt ttgggttctt tctagaagat tgagaaatgc atatgacagg ctgagancac 240  
 ctcccaaac acacaagctc tcagccacan gcagcttctc cacagcccca gcttcgcaca 300  
 ggctcctgga ngctgcctg ggggaggcag acatgggagt gccaaagtg ccagatgggt 360  
 ccaggactac aatgtcttta tttttaactg tttgccactg ctgccctcac ccctgcccgg 420  
 ctctggagta ccgtctgccc canacaagtg ggantgaaat ggggggtggg ggggaactg 480  
 attoccantt aggggggtgcc taactgaaca gtagggatan aagggtgtgaa cctngaan 540

```

gcttttataa attatnttcc ttgttanatt tatttttttaa tttaatctct gttnaactgc      600
ccngggaaaaa ggggaaaaaaa aaaaaaaaaat tctnttttaa cacatgaaca      650

```

```

<210> 51
<211> 545
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(545)
<223> n = A,T,C or G

```

```

<400> 51
tggcgtgcaa ccagggtagc tgaagtttgg gtctgggact ggagattggc cattaggcct      60
cctganattc cagctccctt ccaccaagcc cagtcttgct acgtggcaca gggcaaacct      120
gactcccttt gggcctcagt ttcccctccc cttcatgana tgaaaagaat actacttttt      180
cttggttggtc taacnttgct ggacncaaag tgtngtcatt attgttgtat tgggtgatgt      240
gtncaaaaact gcagaagctc actgcctatg agaggaanta agagagatag tggatganag      300
ggacanaagg agtcattatt tggatatagat ccaccntcc caacctttct ctcctcagtc      360
cctgcncctc atgtntctgg tntggtgagt cctttgtgcc accanccatc atgctttgca      420
ttgctgccat cctgggaagg gggtnatcg tctcacaact tgttgtcatc gtttganatg      480
catgctttct tnatnaaaca aanaaannaa tgtttgacag ngtttaaaat aaaaaanaaa      540
caaaa      545

```

```

<210> 52
<211> 678
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(678)
<223> n = A,T,C or G

```

```

<400> 52
actagtagaa gaactttgccc gcttttgtgc ctctcacagg cgcctaaagt cattgccatg      60
ggagggaagac gatttggggg gggagggggg gggggcangg tccgtggggc tttccctant      120
ntatctccat ntccantggn cnntgtcgcc tcttccctcg tcnattnga anttantccc      180
tggnccccnn nccctctccn ncctnccct cccccctccg ncnccctcnn cttttntan      240
ncttccccat ctcnctccc cctnanngtc ccaacnccgn cagcaatnnc naacttnctc      300
nctcncnccc tccnccggtt cttctnttct cnaentntnc ncnntnccn tgccnntnaa      360
annctctccc cnetgcaanc gattctctcc ctccnennan ctntccactc cntncttctc      420
nncgctctct ntctctcnnc ccacctctcn ccttcgncce cantacnctc nccncccttn      480
cgnntenttn nnntcctcnn accnccnccc tcccttnccc cctcttctcc ccggtntntc      540
tctctccncc nncnccncc cncnccntcc nngcgnccnt ttccgccccn cncnccntt      600
ccttctctc cantccatc cntntnccat nctnccctncc nctcancncc gctnccccn      660
ntctctttca cacngtcc      678

```

```

<210> 53
<211> 502
<212> DNA
<213> Homo sapien

```

```

<220>

```

<221> misc\_feature  
 <222> (1)... (502)  
 <223> n = A,T,C or G

<400> 53  
 tgaagatcct ggtgtcgcca tgggcccgcg ccccgcccgt tgttaccggt attgtaagaa 60  
 caagccgtac ccaaagtctc gtttctgccc aggtgtccct gatgccaaaa ttcgcatttt 120  
 tgacctgggg cggaaaaang caaaantgga tgagtctccg ctttgtggcc acatgggtgtc 180  
 agatcaatat gaggcagctgt cctctgaagc cctgnangct gcccgatttt gtgccaataa 240  
 gtacatggta aaaagtngtg gcnaagatgc ttccatatcc ggggtgcgnt ccaccccttc 300  
 caggtcatcc gcatcaacaa gatgtgtgcc tgtgtggtgg ctgacaggct cccaacaggc 360  
 atgcgaagt ccttttgaaa acccanggca ctgtggccag gggttcacatt gggccaattn 420  
 atcatgttca tccgcaccaa ctgcagaaca angaacntgt naattnaagc cctgcccagg 480  
 gncaanttca aatttcccgg cc 502

<210> 54  
 <211> 494  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (494)  
 <223> n = A,T,C or G

<400> 54  
 actagtccaa gaaaaatatg cttaatgtat attacaaagg ctttgtatat gttaacctgt 60  
 tttaatgccaa aaagtttctt ttgtccacaa ttctcttaag acctcttcag aaagggattt 120  
 gtttgccctta atgaatactg ttgggaaaaa acacagtata atgagtgaag agggcgagaag 180  
 caagaaattt ctacatctta gcgactccaa gaagaatgag tatccacatt tagatggcac 240  
 attatgagga ctttaatctt tcttaaaaca caataatgtt ttcttttttc ttttattcac 300  
 atgatttcta agtatatttt tcatgcagga cagtttttca accttgatgt acagtgactg 360  
 tgtaaattt ttctttcagt ggcaacctct ataatcttta aaatatgggt agcatcttgt 420  
 ctgttttgaa ngggatatga cnatnaatct atcagatggg aaatcctgtt tccaagttag 480  
 aaaaaaaaaa aaaa 494

<210> 55  
 <211> 606  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (606)  
 <223> n = A,T,C or G

<400> 55  
 actagtaaaa agcagcattg ccaaataatc cctaattttc cactaaaaat ataatgaaat 60  
 gatgttaagc tttttgaaaa gtttaggtta aacctactgt tgtagatta atgtatttgt 120  
 tgcttccctt tatctggaat gtggcattag cttttttatt ttaacctctt ttaattctta 180  
 ttcaattcca tgacttaagg ttggagagct aaacactggg atttttggat aacagactga 240  
 cagttttgca taattataat cggcattgta catagaaagg atatggctac cttttgttaa 300  
 atctgcactt tctaaatata aaaaaaggga aatgaagtat aaatcaattt ttgtataatc 360  
 tgtttgaaac atgantttta tttgcttaat attanggctt tgcccttttc tgtagtctc 420  
 ttgggatcct gtgtaaaact gttctcatta aacaccaaac agttaagtcc attctctggt 480

actagctaca aattccgttt catattctac ntaacaattt aaattaactg aaatatttct	540
anatggtcta cttctgtcnt ataaaaacna aacttgantt nccaaaaaaa aaaaaaaaaa	600
aaaaaa	606

&lt;210&gt; 56

&lt;211&gt; 183

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 56

actagtatat ttaaaacttac aggcttattt gtaatgtaaa ccaccatttt aatgtactgt	60
aattaacatg gttataatac gtacaatcct tccctcatcc catcacacaa ctttttttgt	120
gtgtgataaa ctgatttttg tttgcaataa aaccttgaaa aataaaaaaa aaaaaaaaaa	180
aaa	183

&lt;210&gt; 57

&lt;211&gt; 622

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(622)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 57

actagtcact actgtottct ccttgtagct aatcaatcaa tattcttccc ttgcctgtgg	60
gcagtggaga gtgctgctgg gtgtacgctg cacctgcccc ctgagttggg gaaagaggat	120
aatcagtgag cactgttctg ctcagagctc ctgatctacc ccacccccta ggatccagga	180
ctgggtcaaa gctgcatgaa accaggccct ggcagcaacc tgggaatggc tggaggtggg	240
agagaacctg acttctcttt cctctcctt cctccaacat tactggaact ctatcctgtt	300
agggatcttc tgagcttggt tccctgctgg gtgggacaga agacaaagga gaagggangg	360
tctacaanaa gcagcccttc tttgtcctct ggggttaatg agcttgacct ananttcatg	420
gaganaccan aagcctctga tttttaattt ccntnaaatg tttgaagtnt atatntacat	480
atatatatat ctttnaatnt ttgagtcttt gatatgtctt aaaatccant ccctctgccn	540
gaaacctgaa ttaaaacat gaanaaaaat gtttncctta aagatgttan taattaattg	600
aaacttgaaa aaaaaaaaaa aa	622

&lt;210&gt; 58

&lt;211&gt; 433

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 58

gaacaaattc tgattgggta tgtaccgtca aaagacttga agaaatttca tgattttgca	60
gtgtggaagc gttgaaaatt gaaagttact gcttttccac ttgtcatat agtaaagga	120
tcctttcagc tgccagtgtt gaataatgta tcatccagag tgatgttata tgtgacagtc	180
accagcttta agctgaacca ttttatgaat accaaataaa tagacctctt gtactgaaaa	240
catattttgt actttaatcg tgctgcttgg atagaaatat ttttactggg tcttctgaat	300
tgacagtaaa cctgtccatt atgaatggcc tactgttcta ttatttgttt tgacttgaat	360
ttatccacca aagacttcat ttgtgtatca tcaataaagt tgtatgtttc aactgaaaaa	420
aaaaaaaaa aaa	433

&lt;210&gt; 59

&lt;211&gt; 649

<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (649)  
<223> n = A,T,C or G

<400> 59  
actagttatt atctgacttt cngggtataa tcattctaata gagtgtgaag tagcctctgg 60  
tgtcatttgg atttgcatth ctctgatgag tgatgctatc aagcaccttt gctgggtgctg 120  
ttggccatat gtgtatgttc cctggagaag tgtctgtgct gagccttggc ccacttttta 180  
attaggcgtn tgccttttta ttactgagtt gtaaganttc tttatatatt ctggattcta 240  
gacccttata agatacatgg ttgcaaata ttttctccca ttctgtgggt tgtgttttca 300  
ctttatcgat aatgtcctta gacatataat aaatttgtat tttaaaagtg acttgatttg 360  
ggctgtgcaa ggtgggctca cgcttgaat cccagcactt tgggagactg aggtgggtgg 420  
atcatatgan gangctagga gttcgaggtc agcctggcca gcatagcgaa aacttgtctc 480  
tacnaaaat acaaaaatta gtcaggcatg gtggtgcacg tctgtaatac cagcttctca 540  
ggangctgan gcacaaggat cacttgaacc ccagaangaa gangttgcag tganctgaag 600  
atcatgccag ggcaacaaaa atgagaactt gtttaaaaaa aaaaaaaaaa 649

<210> 60  
<211> 423  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (423)  
<223> n = A,T,C or G

<400> 60  
actagttcag gccttcacgt tcaactgacaa acatggggaa gtgtgcccag ctggctggaa 60  
acctggcagt gataccatca agcctgatgt ccaaaagagc aaagaatatt tctccaagca 120  
gaagtgagcg ctgggctgtt ttagtgccag gctgcggtgg gcagccatga gaacaaaacc 180  
tcttctgtat tttttttttc cattagtana acacaagact cngattcagc cgaattgtgg 240  
tgtcttacaa ggcagggtct tcctacaggg ggtgganaaa acagcctttc ttcctttggt 300  
aggaatggcc tgagttggcg ttgtgggcag gctactggtt tgtatgatgt attagtagag 360  
caacccatta atcttttcta gtttgtatna aacttganct gagaccttaa acaaaaaaaaaa 420  
aaa 423

<210> 61  
<211> 423  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (423)  
<223> n = A,T,C or G

<400> 61  
cgggactgga atgtaaagtg aagtccggag ctctgagcac gggctcttcc cgccgggtcc 60  
tccctcccca gacccagag ggagaggccc accccgccc gccccgcccc agccctgtct 120  
caggtctgag tatggctggg agtcgggggc cacaggcctc tagctgtgct gctcaagaag 180



actggatcag	ggtanctaca	agtggccggg	ccttgccctt	gggattctac	cctgttccta	240
atttgggtgt	gggggtgcggg	gtccctggcc	cccttttcca	cactncctcc	ctcngacag	300
caacctccct	tggggcaatt	gggcctggnt	ctcncccgn	tgttgcnacc	ctttgttggt	360
ttaaggnttt	taaaaatggt	annttttccc	ntgcncgggt	taaaaaagga	aaaaactnaa	420
aaa						423

```
<210> 62
<211> 683
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1) ... (683)
<223> n = A,T,C or G
```

<400> 62							
gctggagagg	ggtacggact	ttcttggagt	tgtcccaggt	tggaatgaga	ctgaactcaa		60
gaagagaccc	taagagactg	gggaatggtt	cctgccttca	ggaaagtgaa	agacgcttag		120
gctgtcaaca	cttaaaggaa	gtccccttga	agcccagagt	ggacagacta	gacccattga		180
tggggccact	ggccatggtc	cgttgacaag	acattccngt	gggccaatgg	acaccggggg		240
ggatcaaaaat	gtgtacttgt	ggggctctgc	cccttgccaa	aaccaaacca	ntcccactcc		300
tgtcnttggga	ctttcttccc	attccctect	ccccaaatgc	acttcccctc	ctccctctgc		360
ccctcctgtg	tttttggaaat	tctgtttccc	tcaaaattgt	taatttttta	nttttngacc		420
atgaacttat	gtttggggtc	nangttcccc	ttnccaatgc	atactaatat	attaatgggt		480
atttattttt	gaaatatttt	ttaatgaact	tggaaaaaat	tnntggaatt	tccttncttc		540
cnttttnttt	gggggggggtg	gggggntggg	ttaaaatttt	tttggaancc	cnatnggaaa		600
ttnttacttg	gggcccctct	naaaaaaantn	antccaatt	cttnnatngc	ccctnttccn		660
ctaaaaaaaaa	ananannaaa	aan					683

```
<210> 63
<211> 731
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G
```

<400> 63							
actagtcata	aaggggtgtgc	gcgtcttctga	cgtggcggtc	ttggcgccac	tgctgcgaga		60
cccggccctg	gacctcaagg	tcattccactt	ggtgctgat	ccccgcgcgg	tggcgagttc		120
acggatccgc	tcgcgccacg	gcctcatccg	tgagagccta	caggtggtgc	gcagccgaga		180
ccgcgagctc	accgcatgcc	cttcttggag	gccgcggggc	acaagcttgg	cgcccanaaa		240
gaaggcgtng	ggggcccgca	aantaccacg	ctctgggcgc	tatggaangt	cctcttgcaa		300
taatattggt	tnaaaantctg	canaanagcc	cctgcanccc	cctgaactgg	gntgcagggc		360
cncttacctn	gtttggtgtc	ggttacaaag	aacctgttn	ggaaaacct	ncnaaaacc		420
ttccgggaaa	attntncaaa	ttttnttgg	ggaattnttg	ggtaaacc	ccnaaatgg		480
gaaacntttt	tgccctnaa	antaaccat	tnggttccgg	gggcccccc	ncaaaccct		540
ttttntttt	ttntgcccc	cantncccc	ccggggcccc	tttttttngg	ggaaaanccc		600
ccccctncc	nanantttta	aaagggnggg	anaatttttn	ntncccccc	gggncccccn		660
ggngntaaaa	nggtttcncc	cccccgaggg	gnggggnnnc	ctcnnaaac	cntntcnna		720
cnctnttttn	ng						731

<210> 64  
<211> 313  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(313)  
<223> n = A,T,C or G

<400> 64  
actagttgtg caaaccacga ctgaagaaag acgaaaagtg ggaaataact tgcaacgtct 60  
gttagagatg gttgctacac atgttgggtc tgtagagaaa catcttgagg agcagattgc 120  
taaagttgat agagaatatg aagaatgcat gtcagaagat ctctcggaat atattaaaga 180  
gattagagat aagtatgaga agaaagctac tctaattaag tcttctgaag aatgaagatn 240  
aaatgttgat catgtatata tatccatagt gaataaaatt gtctcagtaa agttgtaaaa 300  
aaaaaaaaaa aaa 313

<210> 65  
<211> 420  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(420)  
<223> n = A,T,C or G

<400> 65  
actagttccc tggcaggcaa gggcttccaa ctgaggcagt gcatgtgtgg cagagagagg 60  
caggaagctg gcagtggcag cttctgtgtc tagggagggg tgtggctccc tecttcctg 120  
tctgggaggt tggaggggaag aatctaggcc ttagcttgcc ctctgccac cttcccctt 180  
gtagatactg ccttaacact cctcctctc tcagctgtgg ctgccacca agccagggtt 240  
ctcgtgtctc actaatttat ttccaggaaa ggtgtgtgga agacatgagc cgtgtataat 300  
atttgtttta acattttcat tgcaagtatt gaccatcatc cttggtgtg tctcgttgta 360  
acacaaatta atgatattaa aaagcatcca aacaaagccn annnnnaana nnnnnngaaa 420

<210> 66  
<211> 676  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(676)  
<223> n = A,T,C or G

<400> 66  
actagtttcc tatgatcatt aaactcattc tcagggttaa gaaaggaatg taaatttctg 60  
cctcaatttg tacttcatca ataagttttt gaagagtgca gatttttagt caggtcttaa 120  
aaataaaactc acaaactctg atgcatttct aaattctgca aatgtttcct ggggtgactt 180  
aacaaggaat aatcccacaa tatacctagc tacctaatac atggagctgg ggctcaaccc 240  
actgttttta aggatttgcg cttacttgtg gctgaggaaa aataagtagt tccgagggaa 300  
gtagttttta aatgtgagct tatagatngg aaacagaata tcaacttaat tatggaaatt 360  
gttagaaacc tgttctcttg ttatctgaat cttgattgca attactattg tactggatag 420

```

actccagccc attgcaaagt ctcagatata ttanctgtgt agttgaattc cttggaaatt    480
ctttttaaga aaaaattgga gtttnaaaga aataaacccc tttgttaaata gaagcttggc    540
tttttggtga aaaanaata tccccagggg cttattgttt aaaaanggaa ttttaagcct    600
ccctggaaaa anttgtaata taaatgggga aaatgntggg naaaaattat ccgttagggg    660
ttaaagggaa aactta                                     676

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<210> 67
<211> 620
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (620)
<223> n = A,T,C or G

```

```

<400> 67
caccattaaa gctgcttacc aagaacttcc ccagcatttt gacttccttg tttgatagct    60
gaattgtgag cagggtgatag aagagccttt ctagtgaac atacagataa tttgctgaat    120
acattccatt taatgaagg gttacatctg ttacgaagct actaagaagg agcaagagca    180
taggggaaaa aaatctgac agaacgcac aaactcacat gtgccccctc tactacaaac    240
agattgtagt gctgtggtgg tttattccgt tgtgcagaac ttgcaagctg agtcactaaa    300
cccaaagaga ggaaattata ggtagttaa acattgtaat ccaggaact aagtttaatt    360
cacttttgaa gtgttttgtt ttttattttt ggttgtctg atttactttg ggggaaaang    420
ctaaaaaaaa agggatatca atctctaatt cagtgccac taaaagtgt ccctaaaaag    480
tctttactgg aanttattgg actttttaag ctccaggnt tttggtcctc caaattaacc    540
ttgcatgggc cccttaaaat tgtgaangg cattcctgcc tctaagtttg gggaaaattc    600
ccccnttttn aaaatttgga                                     620

```

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<210> 68
<211> 551
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (551)
<223> n = A,T,C or G

```

```

<400> 68
actagtagct ggtacataat cactgaggag ctatttctta acatgctttt atagaccatg    60
ctaagtctag accagtattt aagggtctaat ctcacacctc cttagctgta agagtctggc    120
ttagaacaga cctctctgtg caataacttg tggccactgg aaatccctgg gccggcattt    180
gtattggggg tgcaatgact cccaagggcc aaaagagtta aaggcacgac tgggatttct    240
tctgagactg tggtgaaact ccttccaagg ctgagggggg cagtangtgc tctgggaggg    300
actcggcacc actttgatat tcaacaagcc acttgaagcc caattataaa attgttattt    360
tacagctgat ggaactcaat ttgaaccttc aaaactttgt tagtttatcc tattatattg    420
ttaaaccata ttacatttgt ctagcattgg atttgggtcc tgtngcatat gttttttcn    480
cctatgtgct cccctcccc nnatcttaat ttaaaccnca attttgcnat tcnccnnnnn    540
nannnnanna a                                     551

```

```

<210> 69
<211> 396
<212> DNA
<213> Homo sapien

```

<220>  
 <221> misc\_feature  
 <222> (1)...(396)  
 <223> n = A,T,C or G

<400> 69  
 cagaaatgga aagcagagtt ttcattttctg tttataaaacg tctccaaaca aaaatggaaa 60  
 gcagagtttt cattaaatcc ttttaccttt tttttttctt ggtaatcccc tcaaataaca 120  
 gtatgtggga tattgaatgt taaagggata tttttttcta ttatttttat aattgtacaa 180  
 aattaagcaa atgttaaaag ttttatatgc tttattaatg ttttcaaaag gtatnataca 240  
 tgtgatacat tttttaagct tcagttgctt gtcttctggt actttctggt atgggctttt 300  
 ggggagccan aaaccaatct acnatctctt tttgtttgcc aggacatgca ataaaattta 360  
 aaaaataaat aaaaactatt nagaaattga aaaaaa 396

<210> 70  
 <211> 536  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(536)  
 <223> n = A,T,C or G

<400> 70  
 actagtgcga aagcaaatat aaacatcgaa aaggcggtcc tcacgttagc tgaagatata 60  
 cttegaaaga cccctgtaaa agagcccaac agtgaaaatg tagatatcag cagtggagga 120  
 ggcgtgacag gctggaagag caaatgctgc tgagcattct cctgttccat cagttgccat 180  
 ccactacccc gttttctctt cttgctgcaa aataaaccac tctgtccatt ttttaactcta 240  
 aacagatatt tttgtttctc atcttaacta tccaagccac ctattttatt tgttctttca 300  
 tctgtgactg cttgctgact ttatcataat tttcttcaaa caaaaaaatg tatagaaaaa 360  
 tcatgtctgt gacttcattt ttaaagtnta cttgctcagc tcaactgcat ttcagttggt 420  
 ttatagtcca gttcttatca acattnaaac ctatngcaat catttcaaat ctattctgca 480  
 aattgtataa gaataaaagt tagaatttaa caattaaaaa aaaaaaaaaa aaaaaa 536

<210> 71  
 <211> 865  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(865)  
 <223> n = A,T,C or G

<400> 71  
 gacaaagcgt taggagaaga anagaggcag ggaanactnc ccaggcacga tggccnctt 60  
 cccaccagca accagcgccc cccaccagcc cccaggcccg gacgacgaag actccatcct 120  
 ggattaatct nacctctntc gectgnocca ttcctacctc ggaggtggag gccggaaagg 180  
 tcncaccaag aganaantcgt ctgccaacac caaccgcccc agccctggcg ggcacganag 240  
 gaaactggtg accaatctgc agaattctna gaggaanaag cnagggggccc cgcgctnaga 300  
 cagagctgga tatgangcca gaccatggac nctacnccn ncaatncana cgggactgcg 360  
 gaagatggan gaccncgac nngatcaggc cngctnncca nccccacc cctatgaatt 420  
 attcccgtcg aangaatctc tgannggett ccannaaagc gcctccccnc cnaacgnaan 480

tncaacatng	ggattanang	ctgggaactg	naaggggcaa	ancctnnaat	atccccagaa	540
acaanctctc	ccnaanaaac	tggggcncct	catnggtggn	accaactatt	aactaaaccg	600
cacgccaagn	aantataaaa	ggggggcccc	tccncggng	acccccctttt	gtcccttaat	660
ganggttatc	cnccttgctg	accatggtn	ccnnttctgt	ntgnatgttt	ccnctcccc	720
ccnctatnt	cnagccgaac	tcnnatttnc	cggggggtgc	nacnntng	tnncctttt	780
ttngttgncc	cngcccttcc	cgnccgaacn	cgtttccccg	ttantaacgg	caccggggg	840
aagggtgntt	ggccccctcc	ctccc				865

<210> 72  
 <211> 560  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (560)  
 <223> n = A,T,C or G

<400> 72						
cctggacttg	tcttggttcc	agaacctgac	gaccggcgga	cggcgacgtc	tcttttgact	60
aaaagacagt	gtccagtgtc	ccngcctagg	agtctacggg	gaccgcctcc	cgcgcgccca	120
ccatgcccaa	cttctctggc	aactggaaaa	tcacccgac	ggaaaacttc	gangaattgc	180
tcnaantgct	gggggtgaat	gtgatgctna	ngaanattgc	tgtggctgca	gcgtccaagc	240
cagcagtggg	gacnaaacag	gagggagaca	ctttctacat	caaaacctcc	accaccgtgc	300
gcaccacaaa	gattaacttc	nnngttgggg	aggantttga	ggancaaact	gtggatngga	360
ngcctgtnaa	aacctggtga	aatgggagaa	tganaataaa	atggtctgtg	ancanaaact	420
cctgaaagga	gaaggcccc	anaactcctg	gaccngaaaa	actgaccnc	cnatngggga	480
actgatnctt	gaacctgaa	cgggcgggat	ganccttttt	tnttgccncc	naanggggtc	540
tttccntttc	ccccaaaaaa					560

<210> 73  
 <211> 379  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (379)  
 <223> n = A,T,C or G

<400> 73						
ctggggancc	ggcggtngc	nccatntcnn	gncgcgaagg	tggcaataaa	aanccnctga	60
aaccgcnaaa	naaacatgcc	naagatatgg	acgaggaaga	tngngctttc	nngnacaanc	120
gnannagga	acanaacaaa	ctcnangagc	tctcaagcta	atgccgcggg	gaagggggcc	180
ttggccacnn	gtggaattaa	gaaatctggc	aaanngtann	tgttccttgt	gcctnangag	240
ataaangacc	ctttatttca	tctgtattta	aacctctctn	ttccctgnca	taacttcttt	300
tnccacgtan	agntggaant	antgtgtgtc	ttggactgtt	gtncatttta	gannaaactt	360
ttgttcaaaa	aaaaaataa					379

<210> 74  
 <211> 437  
 <212> DNA  
 <213> Homo sapien

<220>

<221> misc\_feature  
<222> (1)...(437)  
<223> n = A,T,C or G

<400> 74  
actagttcag actgccacgc caaccccgaga aaatacccca catgccagaa aagtgaagtc 60  
ctaggtgttt ccattctatgt ttcaatctgt ccattctacca ggcctcgcga taaaaacaaa 120  
acaaaaaaaaac gctgccaggt tttanaagca gttctggctc caaaaccatc aggatcctgc 180  
caccagggtt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcatct 240  
aatcactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgttgagg 300  
gaataagtta taatcagtat tcattctcttt gttttttgtc actcttttct ctctnattgt 360  
gtcatttgta ctgtttgaaa aatatttctt ctataaaatt aaactaacct gccttaaaaa 420  
aaaaaaaaaa aaaaaaaa 437

<210> 75  
<211> 579  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(579)  
<223> n = A,T,C or G

<400> 75  
ctccgtcgcc gccaaagatga tgtgcggggc gccctccgcc acgcagccgg ccaccgccga 60  
gaccagcac atcgccgacc aggtgaggtc ccagcttgaa gagaaagaaa acaagaagtt 120  
ccctgtgttt aaggcctgtt cattcaagag ccagggtgtc gcggggacaa actacttcat 180  
caagggtcac gtcggcgacg aggacttcgt acacctgcga gtgttccaat ctctccctca 240  
tgaaaacaag cccttgacct tatctaacta ccagaccaac aaagccaagc atgatgagct 300  
gacctatttc tgatcctgac ttgggacaag gcccttcagc cagaagactg acaaagtcat 360  
cctccgtcta ccagagcgtg cacttgtgat cctaaaataa gtttcatctc cgggctgtgc 420  
ccttgggggtg gaaggggcan gatctgcact gcttttgcatt ttctcttctt aaatttcatt 480  
gtgttgattc ttctcttcca ataggtgatc ttnattactt tcagaatatt ttccaaatna 540  
gatataatatt naaaatcctt aaaaaaaaaa aaaaaaaaaa 579

<210> 76  
<211> 666  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(666)  
<223> n = A,T,C or G

<400> 76  
gtttatccta tctctocaac cagattgtca gtccttgag ggcaagagcc acagtatatt 60  
tcctgttttc ttccacagtg cctaataata ctgtggaact aggttttaatt aatttttta 120  
ttgatgttgt tatgggcagg atggcaacca gaccattgtc tcagagcagg tgctggctct 180  
ttctgggcta ctccatgttg gctagcctct ggtaacctct tacttattat cttcaggaca 240  
ctcactacag ggaccaggga tgatgcaaca tccttgtctt tttatgacag gatgtttgct 300  
cagcttctcc aacaataaaa agcacgtggg aaaacacttg cggatattct ggactgtttt 360  
taaaaaatat acagtttacc gaaaatcata ttatcttaca atgaaaagga ntttatagat 420  
cagccagtg acaacctttt cccaccatac aaaaattcct tttcccgaa gaaaanggct 480

ttctcaataa	ncctcacttt	cttaanatct	tacaagatag	ccccganatc	ttatcgaaac	540
tcatttttagg	caaatatgan	ttttattgtn	cgttacttgt	ttcaaaat	ggtattgtga	600
atatcaatta	ccaccccat	ctcccatgaa	anaaanggga	aanggtgaan	ttcntaancg	660
cttaaa						666

&lt;210&gt; 77

&lt;211&gt; 396

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(396)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 77

ctgcagcccg	ggggatccac	taatctacca	nggttat	gcagctaatt	ctanatttgg	60
atcattgccc	aaagttgcac	ttgctggtct	cttgggattt	ggccttggaa	aggtatcata	120
catanganta	tgccanaata	aattccattt	ttttgaaaat	canctcctng	gggctggttt	180
tggtccacag	cataacangc	actgcctcct	tacctgtgag	gaatgcaaaa	taaagcatgg	240
attaagttag	aaggagact	ctcagccttc	agcttcctaa	attctgtgtc	tgtgactttc	300
gaagtttttt	aaacctctga	atttgtacac	atttaaaatt	tcaagtgtac	tttaaaataa	360
aatacttcta	atgggaacaa	aaaaaaaaaa	aaaaaa			396

&lt;210&gt; 78

&lt;211&gt; 793

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(793)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 78

gcacccctagc	cgccgactca	cacaaggcag	gtgggtgagg	aaatccagag	ttgccatgga	60
gaaaattcca	gtgtcagcat	tcttgcctct	tgtggccctc	tcctacactc	tgccagaga	120
taccacagtc	aaacctggag	ccaaaaagga	cacaaaaggac	tctcgaccca	aactgccccca	180
gacctctcc	agaggttggg	gtgaccaact	catctggact	cagacatatg	aagaagctct	240
atataaatcc	aagacaagca	acaaaccctt	gatgattatt	catcacttgg	atgagtgtccc	300
acacagtcna	gctttaaaga	aagtgtttgc	tgaaaataaa	gaaatccaga	aattggcaga	360
gcagtttgtc	ctcctcaatc	tggtttatga	aacaactgac	aaacaccttt	ctcctgatgg	420
ccagtatgtc	ccaggattat	gtttgttgac	ccatctctga	cagttgaagc	cgatatcctg	480
ggaagatatt	cnaaccgtct	ctatgcttac	aaactgcaga	tacgctctgt	tgttgacac	540
atgaaaaagc	tctcaagttg	ctnaaaatga	attgtaaaga	aaaaaatctc	cagccttctg	600
tctgtcggct	tgaaaattga	aaccagaaaa	atgtgaaaaa	tggctattgt	ggaacanatn	660
gacacctgat	taggttttgg	ttatgttcac	cactattttt	anaaaanan	nttttaaaat	720
ttggttcaat	tntctttttn	aaacaatntg	tttctacntt	gnganctgat	ttctaaaaaa	780
aataatnttt	ggc					793

&lt;210&gt; 79

&lt;211&gt; 456

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(456)  
 <223> n = A,T,C or G

<400> 79  
 actagtatgg ggtgggaggg cccacccttc tcccctaggg gctgttcttg ctccaaaggg 60  
 ctccgtggag agggactggc agagctgang ccacctgggg ctggggatcc cactcttctt 120  
 gcagctgttg agcgcaccta accactgggc atgccccac cctgtctctc cgcaccgct 180  
 tcctcccgac cccangacca ggctacttct cccctcctct tgcctccctc ctgcccctgc 240  
 tgctctgat cgtangaatt gangantgtc cgccttggg gctganaatg gacagtggca 300  
 ggggctggaa atgggtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt gcnccccccc 360  
 tgcaagaccg agattgaggg aaancatgtc tgctgggtgt gaccatgttt cctctccata 420  
 aantnccccct gtgacnctca naaaaaaaaa aaaaaa 456

<210> 80  
 <211> 284  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(284)  
 <223> n = A,T,C or G

<400> 80  
 ctttgtacct ctagaaaaga taggtattgt gtcataaaac ttgagtttaa attttatata 60  
 taaaactaaa agtaatgtct acttttagcaa cacatactaa aattggaacc atactgagaa 120  
 gaatagcatg acctccgtgc aaacaggaca agcaaatttg tgatgtgttg attaaaaaga 180  
 aataaataaa tgtgtatatg tgtaacttgt atgtttatgt ggaatacaga ttgggaaata 240  
 aaatgtattt cttactgtga aaaaaaaaaa aaaaaaaaaa aana 284

<210> 81  
 <211> 671  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(671)  
 <223> n = A,T,C or G

<400> 81  
 gccaccaaca ttccaagcta ccctgggtac ctttgtgcag tagaagctag tgagcatgtg 60  
 agcaagcggg gtgcacacgg agactcatcg ttataattta ctatctgcca agagtagaaa 120  
 gaaaggctgg ggatatttgg gttggcttgg ttttgatttt ttgcttgttt gtttgttttg 180  
 tactaaaaca gtattatctt ttgaatatcg tagggacata agtatataca tgttatccaa 240  
 tcaagatggc tagaatgggt cctttctgag tgtctaaaac ttgacacccc tggtaaattct 300  
 ttcaacacac ttccactgcc tgcgtaatga agttttgatt catttttaac cactggaatt 360  
 tttcaatgcc gtcattttca gttagatnat tttgcacttt gagattaaaa tgccatgtct 420  
 atttgattag tcttattttt ttattttttac aggcttatca gtctcactgt tggctgtcat 480  
 tgtgacaaaag tcaataaaac ccccnaggac aacacacagt atgggatcac atattgtttg 540  
 acattaagct ttggccaaaa aatgttgcac gtgttttacc tcgacttgct aaatcaatan 600  
 canaaaggct ggctnataat gttgggtgtg aaataattaa tnantaacca aaaaaaaaaa 660  
 aaaaaaaaaa a 671



<210> 82  
 <211> 217  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (217)  
 <223> n = A,T,C or G

<400> 82  
 ctgcagatgt ttcttgaatg ctttgtcaaa ttaanaaaagt taaagtcaa taatgtttga 60  
 agacaataag tgggtgtgta tcttgtttct aataagataa acttttttgt ctttgcttta 120  
 tcttattagg gagttgtatg tcagtgtata aaacatactg tgtggtataa caggcttaat 180  
 aaattcttta aaaggaaaaa aaaaaaaaaa aaaaaaa 217

<210> 83  
 <211> 460  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (460)  
 <223> n = A,T,C or G

<400> 83  
 cgcgagtggg agcaccagga tctcgggctc ggaacgagac tgcacggatt gttttaagaa 60  
 aatggcagac aaaccagaca tgggggaaat cgccagcttc gatnaggcca agctgaanaa 120  
 aacggagacg caggagaaga acaccctgcc gaccaaagag accattgagc angagaagcg 180  
 gagtgaaatt tcctaagatc ctggaggatt tcctaccccc gtcctcttcg agaccccgat 240  
 cgtgatgtgg aggaagagcc acctgcaaga tggacacgag ccacaagctg cactgtgaac 300  
 ctgggcactc cgcgccgatg ccaccggcct gtgggtctct gaagggaccc cccccaatcg 360  
 gactgcaaaa ttctccggtt tgccccggga tattatacaa nattatttgt atgaataatg 420  
 annataaaac acacctcgtg gcancaaana aaaaaaaaaa 460

<210> 84  
 <211> 323  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (323)  
 <223> n = A,T,C or G

<400> 84  
 tgggtgatct tggctctgtg gagctgctgg gacgggatct aaaagactat tctggaagct 60  
 gtgggtccaan gcattttgct ggcttaacgg gtccccgaac aaaggacacc agctctctaa 120  
 aattgaagtt taccganat aacaatcttt tgggcagaga tgcctatttt aacaaacncc 180  
 gtccctgcgc aacaacnaac aatctctggg aaataccggc catgaacntg ctgtctcaat 240  
 cnancatctc tctagctgac cgatcatatc gtcccagatt actacanatc ataataattg 300  
 atttctgtga naaaaaaaaaa aaa 323

<210> 85  
 <211> 771  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(771)  
 <223> n = A,T,C or G

<400> 85  
 aaactgggta ctcaacactg agcagatctg ttctttgagc taaaaaccat gtgctgtacc 60  
 aanagtttgc tcctggctgc tttgatgtca gtgctgtac tccacctctg cggcgaatca 120  
 gaagcaagca actttgactg ctgtcttgga tacacagacc gtattcttca tcctaaattt 180  
 attgtgggct tcacacggca gctggccaat gaaggctgtg acatcaatgc tatcatcttt 240  
 cacacaaaga aaaagttgtc tgtgtgcgca aatccaaaac agacttgggt gaaatatatt 300  
 gtgcgtctcc tcagtaaaaa agtcaagaac atgtaaaaac tgtggctttt ctggaatgga 360  
 attggacata gcccaagaac agaaagaact tgctgggggt ggaggtttca cttgcacatc 420  
 atgganggtt tagtgcttat cttatttgtg cctcctggac ttgtccaatt natgaagtta 480  
 atcatattgc atcatanttt gctttgttta acatcacatt naaattaaac tgtattttat 540  
 gttattttata gctntaggtt ttctgtgttt aactttttat acnaantttc ctaaactatt 600  
 ttggnttant gcaanttaaa aattatattt ggggggggaa taaatattgg antttctgca 660  
 gccacaagct ttttttaaaa aaccantaca nccnngttaa atggtnggtc ccnaatgggt 720  
 tttgcttttn antagaaaat ttnttagaac natttgaaaa aaaaaaaaaa a 771

<210> 86  
 <211> 628  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(628)  
 <223> n = A,T,C or G

<400> 86  
 actagtttgc tttacatttt tgaaaagtat tatttttgtc caagtgttta tcaactaaac 60  
 cttgtgttag gtaagaatgg aatttattaa gtgaatcagt gtgaccttc ttgtcataag 120  
 attatcttaa agctgaagcc aaaatatgct tcaaaagaaa angactttat tgttcattgt 180  
 agttcatata ttcaaagcat ctgaactgta gtttctatag caagccaatt acatccataa 240  
 gtggagaang aaatagatta atgtcnaagt atgattggtg gagggagcaa ggttgaagat 300  
 aatctggggt tgaaattttc tagttttcat tctgtacatt tttagttnga catcagattt 360  
 gaaatattaa tgtttacctt tcaatgtgtg gtatcagctg gactcantaa cacccttttc 420  
 ttccctnggg gatggggaat ggattattgg aaaatggaaa gaaaaaagta cttaaagcct 480  
 tccttttncg gtttctggct cctaccctac tgatttancc agaataagaa aacattttat 540  
 catcntctgc tttattccca ttaatnaant tttgatgaat aaatctgctt ttatgcnnac 600  
 ccaaggaatt nagtggnttc ntcnttgt 628

<210> 87  
 <211> 518  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature

&lt;222&gt; (1) ... (518)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 87

ttttttat	tttttagaga	gtagttcagc	ttttat	aaatttattg	cctgttttat	60
tataacaaca	ttatactgtt	tatggtttaa	tacatatggt	tcaaaatgta	taatacatca	120
agtagtacag	ttttaaaatt	ttatgcttaa	aacaagtttt	gtgtaaaaaa	tcagataca	180
ttttacatgg	caaatcaatt	tttaagtcac	cctaaaaatt	gatttttttt	tgaaatttaa	240
aaacacattt	aatttcaatt	tctctcttat	ataaccttta	ttactatagc	atgggttcca	300
ctacagttta	acaatgcagc	aaaattccca	tttcacggta	aattgggttt	taagcggcaa	360
ggttaaaatg	ctttgaggat	cctnaatacc	ctttgaactt	caaataaggg	ttatggttgt	420
naatttaacc	ctcatgccat	aagcagaagc	acaagtttag	ctgcattttg	ctctaaactg	480
taaaaacgag	cccccggtg	aaaaagcaaa	agggaccc			518

&lt;210&gt; 88

&lt;211&gt; 1844

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 88

gagacagtga	atcctagtat	caaaggattt	ttggcctcag	aaaaagttgt	tgattat	60
tattttat	tatttttoga	gactccgtct	caaaaaaaa	aaaaaaaaa	agaatcaca	120
ggtatttgct	aaagcatttt	gagctgcttg	gaaaaagggg	agtagttgca	gtagagtttc	180
ttccatcttc	ttggtgctgg	gaagccatat	atgtgtcttt	tactcaagct	aaggggtata	240
agcttatgtg	ttgaatttgc	tacatctata	tttcacatat	tctcacaata	agagaat	300
gaaatagaaa	tatcatagaa	catttaagaa	agtttagtat	aaataatatt	ttgtgtgttt	360
taatcccttt	gaagggatct	atccaaagaa	aatattttac	actgagctcr	ttcctacacg	420
tctcagtaac	agatcctgtg	ttagtctttg	aaaatagctc	attttttaaa	tgtcagtggg	480
tagatgtagc	atacatatga	tgtataatga	cgtgtattat	gttaacaatg	tctgcagatt	540
ttgtaggaat	acaaaacatg	gcctttttta	taagcaaaac	gggccaatga	ctagaataac	600
acatagggca	atctgtgaat	atgtattata	agcagcattc	cagaaaagta	ggtggtgaaa	660
taattttcaa	gtcaaaaagg	gatattggaa	gggaattatg	agtaacctct	attttttaag	720
ccttgctttt	aaattaaacg	ctacagccat	ttaagccttg	aggataataa	agcttgagag	780
taataatggt	agggttagcaa	aggtttagat	gtatcacttc	atgcatgcta	ccatgatagt	840
aatgcagctc	ttcgagtcac	ttctgggtcat	tcaagatatt	cacctttttg	cccatagaaa	900
gcaccctacc	tcacctgctt	actgacattg	tcttagctga	tcacaagatc	attatcagcc	960
tccattattc	cttactgtat	ataaaaataca	gagttttata	ttttcctttc	ttcgtttttc	1020
accatattca	aaacctaaat	ttgtttttgc	agatgggaatg	caaagtaatc	aagtgttcgt	1080
gctttcacct	agaaggggtg	ggtcctgaag	gaaagaggtc	cctaaatata	ccccaccctg	1140
ggtgctcctc	cttccctggg	accctgacta	ccagaagtca	ggtgctagag	cagctggaga	1200
agtgcagcag	cctgtgcttc	cacagatggg	ggtgctgctg	caacaaggct	ttcaatgtgc	1260
ccatcttagg	gggagaagct	agatcctgtg	cagcagcctg	gtaagtcctg	aggaggttcc	1320
attgctcttc	ctgctgctgt	cctttgcttc	tcaacggggc	tcgctctaca	gtctagagca	1380
catgcagcta	acttgtgcct	ctgcttatgc	atgagggtta	aattaacaac	cataaccttc	1440
atttgaagtt	caaaggtgta	ttcaggatcc	tcaaagcatt	ttaaccttgc	cgcttaaaac	1500
ccaatttacc	gtgaaatggg	aattttgctg	cattgtttaa	ctgtagtgga	aaccatgcta	1560
tagtaataaa	ggttatataa	gagagaaatt	gaaattaaat	gtgtttttta	atttcaaaaa	1620
aaaaatcaatc	tttaggtaga	cttaaaaatt	gatttgccat	gtaaaatgta	tctgcatttt	1680
ttacacaaaa	cttgttttaa	gcataaaatt	ttaaaactgt	actacttgat	gtattataca	1740
ttttgaacca	tatgtattaa	accataaaca	gtataatggt	gttataataa	aacaggcaat	1800
aaattttataa	ataaaaagctg	aaaaaaaaaa	aaaaaaaaaa	aaaa		1844

&lt;210&gt; 89

&lt;211&gt; 523

&lt;212&gt; DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(523)

<223> n = A,T,C or G

<400> 89

tttttttttt	tttttttagt	caatccacat	ttattgatca	cttattatgt	accaggcact	60
gggataaaga	tgactgttag	tcactcacag	taaggaagaa	aactagcaaa	taagacgatt	120
acaatatgat	gtagaaaatg	ctaagccaga	gatatagaaa	ggtcctattg	ggtccttctg	180
tcaccttgtc	tttccacatc	cctacccttc	acaggccttc	cctccagctt	cctgcccccg	240
ctccccactg	cagatccctt	gggattttgc	ctagagctaa	acgagganat	gggccccctg	300
gccctggcat	gacttgaacc	caaccacaga	ctgggaaagg	gagcctttcg	anagtggatc	360
actttgatna	gaaaacacat	aggggaattga	agagaaantc	cccaaattggc	caccctgtgct	420
ggtgctcaag	aaaagtttgc	agaatggata	aatgaaggat	caagggaatt	aatanatgaa	480
taattgaatg	gtggctcaat	aagaatgact	ncnttgaatg	acc		523

<210> 90

<211> 604

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(604)

<223> n = A,T,C or G

<400> 90

ccagtgtggt	ggaatgcaaa	gattaccccg	gaagctttcg	agaagctggg	attccctgca	60
gcaaaggaaa	tagccaatat	gtgtcgtttc	tatgaaatga	agccagaccg	agatgtcaat	120
ctcaccacc	aactaaatcc	caaagtcaaa	agcttcagcc	agtttatctc	agagaaccag	180
gggagccttc	aagggtcatgt	agaaaatcag	ctgttcagat	aggcctctgc	accacacagc	240
ctctttcttc	tctgacctt	ttctcttta	cggcacaaca	ttcatgtttg	acagaacatg	300
ctggaatgca	attgtttgca	acaccgaagg	atttcctgcy	gtcgctctt	cagtagggaag	360
cactgcattg	gtgataggac	acggtaattt	gattcacatt	taacttgcta	gttagtgata	420
aggggtggta	cacctgtttg	gtaaaatgag	aagcctcgga	aacttgggag	cttctctcct	480
accactaatg	gggagggcag	attattactg	ggattttctc	tgggggtgaat	taatttcaag	540
ccctaattgc	tgaaattccc	ctnggcaggc	tccagttttc	tcaactgcat	tgcaaaattc	600
cccc						604

<210> 91

<211> 858

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(858)

<223> n = A,T,C or G

<400> 91

tttttttttt	ttttttttta	tgattattat	tttttttatt	gatctttaca	tcctcagtgt	60
tggcagagtt	tctgatgctt	aataaacatt	tgttctgac	agataagtgg	aaaaaattgt	120
catttcctta	ttcaagccat	gcttttctgt	gatattctga	tcctagtgtga	acatacagaa	180

ataaatgtct	aaaacagcac	ctcgattctc	gtctataaca	ggactaagtt	cactgtgac	240
ttaaataaagc	ttggctaaaa	tgggacatga	gtggaggtag	tcacacttca	gcgaagaaag	300
agaatctcct	gtataatctc	accaggagat	tcaacgaatt	ccaccacact	ggactagtgg	360
atcccccg	ctgcaggaat	tcgatataca	gcttatcgat	accgtcgacc	tcgagggggg	420
gccccgtacc	caattcgccc	tatagtgagt	cgtattacgc	gcgtcactg	gccgtcggtt	480
tacaacgtcg	tgactgggaa	aaccctggcg	ttacccaact	taatcgctt	gcagcacatc	540
cccccttcgc	cagctggcgt	aatagcgaan	agcccgccac	gatcgccctt	ncaacagttg	600
cgcagcctga	atggcgaatg	ggacgcgccc	tgtagcggcg	cattaaagcg	cggcngggtg	660
tgngggntcc	cccacgtgac	cgntacactt	ggcagcgcc	tacgcgggtc	nttcgctttc	720
ttcccttct	ttctcgacc	gttcgcggg	tttccccg	agctnttaat	cgggggntc	780
cctttanggg	tncnaattaa	nggnttacng	gaccttngan	cccaaaaact	ttgattaggg	840
ggaaggtccc	cgaagggg					858

<210> 92  
 <211> 585  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (585)  
 <223> n = A,T,C or G

<400> 92						
gttgaatctc	ctggtgagat	tatacaggag	attctctttc	ttcgctgaag	tgtgactacc	60
tccactcatg	tcccatttta	gccaagctta	tttaagatca	cagtgaactt	agtcctgtta	120
tagacgagaa	tcgaggtgct	gttttagaca	tttatttctg	tatgttcaac	taggatcaga	180
atatacaga	aaagcatggc	ttgaataagg	aaatgacaat	tttttccact	tatctgatca	240
gaacaaatgt	ttattaagca	tcagaaactc	tgccaacact	gaggatgtaa	agatcaataa	300
aaaaaataat	aatcatnann	naaanannan	nngaagggcg	gccgccaccg	cgggtggagct	360
ccagcttttg	ttccctttag	tgaggggtta	ttgcgcgctt	ggcggttaatc	atgggtcatag	420
ctgtttcctg	tgtgaaattg	ttatccggct	cacaattccn	cncaacatac	gagccgggaa	480
gcntnangtg	taaaagcctg	gggggtgccta	attgagttag	ctnactcaca	ttaattgngt	540
tgcgctccac	ttgcccgctt	ttccantccg	ggaaacctgt	tcgnc		585

<210> 93  
 <211> 567  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (567)  
 <223> n = A,T,C or G

<400> 93						
cggcagtgtt	gctgtctg	tggtccacctt	ggaatctggc	tgaactggct	gggaggacca	60
agactgcggc	tgggggtggc	anggaaggga	accgggggct	gctgtgaagg	atcttggaac	120
ttccctgtac	ccaccttccc	cttgcttcac	gtttgtanag	gaaccttg	ccggccaagc	180
ccagtttct	tgtgtgatac	actaatgtat	ttgctttttt	tgggaaatan	anaaaatca	240
attaaattgc	tantgtttct	ttgaannnnn	nnnnnnnnnn	nnnnnnnggg	ggggncgccc	300
cncggngga	aacnccccct	ttgttccct	ttaattgaaa	ggttaattng	cncncntggc	360
gttaancnt	gggccaanp	tngttncctg	tgntgaaatt	gttnatcccc	tcccaaattc	420
ccccccncc	ttccaaaccc	ggaaancctn	annntgttna	ancccggggg	ggtgcctaan	480
ngnaattnaa	ccnaaccccc	ntttaaatng	nnnttgcn	ccacnngccc	cnccttccca	540

567

```
<210> 94
<211> 620
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(620)
<223> n = A,T,C or G
```

<400> 94						
actagtcaaa	aatgctaaaa	taatttgga	gaaaaatattt	tttaagtagt	gttatagttt	60
catgtttatc	ttttattatg	ttttgtgaag	ttgtgtcttt	tcactaatta	cctatactat	120
gccaatatatt	ccttatatct	atccataaca	tttatactac	atttgttaana	naatgacac	180
gtgaacaatta	acactttata	aggtaaaaat	gaggtttcca	anattttaata	atctgatcaa	240
gttctctgta	tttccaaata	gaaatggactt	gggtctgttaa	gggctaagga	gaagaggaag	300
ataagggttaa	aagttgttaa	tgaccaaaca	ttctaaaaga	aatgcaaaaa	aaaagtttat	360
tttcaagcct	togaactatt	taaggaaaagc	aaaatcattt	cctaaatgca	tatcattttgt	420
gagaattttct	cattaatatc	ctgaatcatt	cattttcacta	aggctcatgt	tnactccgat	480
atgtctcttaa	gaaagtacta	tttcatgggtc	caaacctggt	tgccatantt	gggtaaaaggc	540
tttcccctaa	gtgtgaaant	atttaaaatg	aaattttcct	ctttttaaaa	attctttana	600
agggttaagg	gtgttgggga					620

```
<210> 95
<211> 470
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(470)
<223> n = A,T,C or G
```

<400> 95						
ctcgaccttc	tctgcacagc	ggatgaaccc	tgagcagctg	aagaccagaa	aagccactat	60
nactttntgc	ttaattcang	agcttacang	attcttcaaa	gagtgngtcc	agcatccttt	120
gaaacatgag	ttcttaccag	cagaagcaga	cctttacccc	accacctcag	cttcaacagc	180
agcaggtgaa	acaacccatc	cagcctccac	ctnaggaaat	atttgttccc	acaaccaagg	240
agccatgcca	ctcaaagggt	ccacaacctg	naaacacaaa	nattccagag	ccaggctgta	300
ccaagggtccc	tgagccaggg	ctgtaccaan	gtccctgagc	caggttgtag	caangtcctt	360
gagccaggat	gtaccaagggt	ccctgancca	ggttgtccaa	gggtccctgag	ccaggctaca	420
ccaaggggcct	gngccaggca	gcatacaangt	ccctgaccaa	ggcttatcaa		470

```
<210> 96
<211> 660
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(660)
<223> n = A,T,C or G
```

```

<400> 96
tttttttttt tttttttttt ggaattaaaa gcaatttaat gagggcagag caggaaacat    60
gcattttcttt tcattcgaat cttcagatga accctgagca gccgaagacc agaaaagcca    120
tgaagacttt ctgcttaatt caggggctta caggattctt cagagtgtgt gtgaacaaaa    180
gctttatagt acgtattttt aggatacaaa taagagagag actatggctt ggggtgagaa    240
tgtactgatt acaaggtcta cagacaatta agacacagaa acagatggga agagggtgnc    300
cagcatctgg nggttggtt ctcaagggtt tgtctgtgca ccaaattact tctgcttggn    360
cttctgctga gctgggcctg gagtgacctg tgaaggacat ggctctggta cctttgtgta    420
gcctgncaca ggaacttttg tgatccttg ctcaggaaact ttgatggcac ctggctcagg    480
aaacttgatg aagccttggt caagggacct tgatgcttgc tggctcaggg accttgngn    540
ancctgggct canggacctt tgnncnaacc ttggcttcaa gggacccttg gnacatctg    600
gcnnagggac ccttgggncc aacctggggtc ttnagggacc ctttggntnc nanccttggc    660

```

```

<210> 97
<211> 441
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(441)
<223> n = A,T,C or G

```

```

<400> 97
gggaccatac anagtattcc tctcttcaca ccaggaccag ccactgttgc agcatgagtt    60
cccagcagca gaagcagccc tgcacccac cccctcagct tcagcagcag cagggtgaaac    120
agccttgcca gcctccacct caggaacctt gcaccccaa aaccaaggag ccctgccacc    180
ccaaggtgcc tgagccctgc caccctaaag tgccctgagcc ctgccagccc aaggttccag    240
agccatgcca ccccaagggtg cctgagccct gcccttcaat agtcactcca gcaccagccc    300
agcagaanac caagcagaag taatgtgggt cacagccatg cccttgagga gccggccacc    360
agatgctgaa tccctatccc cattctgtgt atgagtcaca tttgccttgc aattagcatt    420
ctgtctcccc caaaaaaaaa a                                441

```

```

<210> 98
<211> 600
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(600)
<223> n = A,T,C or G

```

```

<400> 98
gtattcctct cttcacacca ggaccagcca ctgttgagc atgagttccc agcagcagaa    60
gcagccctgc atcccacccc ctcagcttca gcagcagcag gtgaaacagc cttgccagcc    120
tccacctcag gaacctatga tccccaaaac caaggagccc tgccacccca aggtgcttga    180
gccctggcac cccaaagtgc ctgagccctg ccagcccaag gttccagagc catgccaccc    240
caaggtgcct gagccctgcc cttcaatagt cactccagca ccagcccagc agaanaccaa    300
gcagaagtaa tgtggtccac agccatgccc ttgaggagcc ggccaccana tgctgaatcc    360
cctatcccat tctgtgtatg agtcccattt gccttgcaat tagcattctg tctcccccaa    420
aaaagaatgt gctatgaagc tttctttcct acacactctg agtctctgaa tgaagctgaa    480
ggctttaant acagantcag ttttcagctg ctcagaattc tctgaagaaa agatttaaga    540
tgaaaggcaa atgattcagc tccttattac cccattaaat tcnctttcaa ttccaaaaaa    600

```

<210> 99  
 <211> 667  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(667)  
 <223> n = A,T,C or G

<400> 99  
 actagtgact gagttcctgg caaagaaatt tgacctggac cagttgataa ctcattgtttt 60  
 accatttaaa aaaatcagtg aaggatttga gctgctcaat tcaggacaaa gcattcgaac 120  
 ggtcctgacg ttttgagatc caaagtggca ggaggtctgt gttgtcatgg tgaactggag 180  
 tttctcttgt gagagttccc tcatctgaaa tcatgtatct gtctcacaaa tacaagcata 240  
 agtagaagat ttgttgaaga catagaaccc ttataaagaa ttattaacct ttataaacat 300  
 ttaaagtctt gtgagcacct gggaattagt ataataacaa tgttnatatt ttgattttac 360  
 attttgtaag gctataattg tatcttttaa gaaaacatac cttggatttc tatgttgaaa 420  
 tggagatttt taagagtttt aaccagctgc tgcagatata ttactcaaaa cagatatagc 480  
 gtataaagat atagtaaag catctcctag agtaatatc acttaacaca ttggaaacta 540  
 ttatttttta gatttgaata tnaatgttat tttttaaaca cttgttatga gttacttggg 600  
 attacatttt gaaatcagtt cattccatga tgcantattc tgggattaga ttaagaaaga 660  
 cggaataa 667

<210> 100  
 <211> 583  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(583)  
 <223> n = A,T,C or G

<400> 100  
 gttttgtttg taagatgac acagtcattg tacactgac taaaggacat atatataacc 60  
 ctttaaaaaa aaaatcactg cctcattctt atttcaagat gaatttctat acagactaga 120  
 tgtttttctg aagatcaatt agacattttg aaaatgattt aaagtgtttt ccttaatgtt 180  
 ctctgaaaac aagtttcttt ttagtattta accaaaaaag tgcctttttt gtcactggat 240  
 tctcctagca ttcattgatt ttttttcata caatgaaatt aaaattgcta aaatcatgga 300  
 ctggctttct gggttgattt caggtaagat gtgtttaagg ccagagcttt tctcagtatt 360  
 tgattttttt ccccaatatt tgatttttta aaaatataca catnggtgct gcatttatat 420  
 ctgctgggtt aaaattctgt catatttcac ttctagcctt ttagttatgg caaatcatat 480  
 tttactttta cttaaagcat ttggttattt ggantatctg gttctannct aaaaaaanta 540  
 attctatnaa ttgaantttt ggtactcnnc catatttgga tcc 583

<210> 101  
 <211> 592  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(592)  
 <223> n = A,T,C or G



```

<400> 101
gtggagacgt acaaagagca gccgctcaag acacctggga agaaaaagaa aggcaagccc      60
gggaaacgca aggagcagga aaagaaaaaa cggcgaactc gctctgcctg gttagactct      120
ggagtgactg ggagtgaggc agaaggggac cacctgtctg acacctccac aacgtcgctg      180
gagctcgatt cacggaggca ttgaaatddd cagcaganac cttccaagga catattgcag      240
gattctgtaa tagtgaacat atggaaagta ttagaaatat ttattgtctg taaatactgt      300
aaatgcattg gaataaaact gtctcccca ttgtctatg aaactgcaca ttggtcattg      360
tgaatatttt tttttttgcc aaggctaata caattattat tatcacattt accataattt      420
attttgtcca ttgatgtatt tttttgttaa atgtatcttg gtgctgctga atttctatat      480
ttttgtaca taatgcnttt anatatacct atcaagtttg ttgataaatg acncaatgaa      540
gtgncncnan ttgngnggtg aatttaatga atgcctaatt ttattatccc aa              592

```

```

<210> 102
<211> 587
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(587)
<223> n = A,T,C or G

```

```

<400> 102
cgctctaagc acttagacta catcagggaa gaacacagac cacatccctg tcctcatgcg      60
gcttatgttt tctggaagaa agtggagacc nagtccttg ctttagggct ccccggtggt      120
gggctgtgca ntccggtcag ggcgggaagg gaaatgcacc gctgcatgtg aacttacagc      180
ccaggcggat gcccctccc ttagcactac ctggcctcct gcacccctc gcctcatgtt      240
cctcccacct tcaanaaatg aanaacccca tgggccagc ccttgccct gggaaccaa      300
ggcagccttc caaaactcag gggctgaagc anactattag ggcaggggct gactttgggt      360
gacactgccc attcctctc agggcagctc angtcaccen ggnctcttga acccagcctg      420
ttcctttgaa aaagggcaaa actgaaaagg gcttttccca naaaaagaaa aaccagggaa      480
ctttgccagg gcttcnntnt taccaaaacn ncttctcnng gatttttaat tccccattng      540
gcctccactt accnggggcn atgccccaaa attaanaatt tcccatc              587

```

```

<210> 103
<211> 496
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(496)
<223> n = A,T,C or G

```

```

<400> 103
anaggactgg ccctacntgc tctctctcgt cctacctatc aatgcccaac atggcagaac      60
ctgcancctt tggncactgc anatggaac ctctcagtgt cttgacatca ccttaccnt      120
gcggtgggtc tccaccacaa ccactttgac tctgtggtcc ctgnanggtg gnttctcctg      180
actggcagga tggaccttan ccnacatata cctctgttcc ctctgctnag anaaagaatt      240
cccttaacat gatataatcc acccatgcaa ntngctactg gccagctac catttaccat      300
ttgcctacag aatttcattc agtctacact ttggcattct ctctggcgat agagtgtggc      360
tgggctgacc gcaaaaggty ccttacacac tggccccac cctcaaccgt tgacncatca      420
gangcttgcc tctccttct gattnncccc catgttggat atcaggggtgc tcnagggatt      480
ggaaaagaaa caaaac

```

<210> 104  
<211> 575  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(575)  
<223> n = A,T,C or G

<400> 104  
gcacctgctc tcaatccnnc tctcaccatg atcctccgcc tgcanaaact cctctgccaa 60  
ctatggangt ggtttcnggg gtggctcttg ccaactggga agaagccgtg gtgtctctac 120  
ctgttcaact cngtttgtgt ctgggggac aactnngggc tatggaagcg gctnaactgt 180  
tgttttggtg gaagggctgg taattggctt tgggaagtng cttatngaag ttggcctngg 240  
gaagttgcta ttgaaagtng ccntggaagt ngntttggtg gggggttttg ctggtggcct 300  
ttgttnaatt tgggtgcttt gtnaatggcg gccccctcnc ctgggcaatg aaaaaaatca 360  
ccnatgcngn aaacctcnac nnaacagcct gggcttcct caccctcgaaa aaagttgctc 420  
ccccccaaa aaaggncaan ccctcaann tggaangttg aaaaaatcct cgaatgggga 480  
nccnnaaaac aaaaancccc cntttcccn gnaanggggg aaataccncc cccccactta 540  
cnaaaaccct tntaaaaaac cccccgggaa aaaaa 575

<210> 105  
<211> 619  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(619)  
<223> n = A,T,C or G

<400> 105  
cactagtagg atagaaacac tgtgtcccga gagtaaggag agaagctact attgattaga 60  
gcctaaccga ggtaactgc aagaagaggc gggatacttt cagctttcca tgtaactgta 120  
tgcataaagc caatgtagtc cagttttctaa gatcatgttc caagctaact gaatccact 180  
tcaatacaca ctcatgaact cctgatggaa caataacagg cccaagcctg tggatgatg 240  
tgcacacttg ctagactcan aaaaaatact actctcataa atgggtggga gtattttggt 300  
gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg 360  
gacatttagt tagtgctttt tatataccag gcatgatgct gaggtagact cttgtgtata 420  
tttccaaatt tttgtacagt cgctgcacat atttgaaatc atatattaag acttccaaaa 480  
aatgaagtcc ctggtttttc atggcaactt gatcagtaaa ggattcncct ctggttggtgta 540  
cttaaaacat ctactatatn gttnanatga aattcctttt ccccnctcc cgaaaaana 600  
aagtggtggg gaaaaaaaa 619

<210> 106  
<211> 506  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(506)  
<223> n = A,T,C or G

```

<400> 106
cattggtnc ttcatttgc ntgggaagtgt nnatctctaa cagtggacaa agttcccngt    60
gccttaaaact ctgtnacact tttgggaant gaaaanttng tantatgata ggttattctg    120
angtanagat gttctggata ccattanatn tgccccngt gtcagaggct catatttgtt    180
tatgtaaag gtaatncatt cgctactatn antcaattng aaatanggtc tttgggttat    240
gaatantnng cagcncanct nanangctgt ctgtngtatt cattgtgggc atagcacctc    300
acancattgt aacctcnatc nagtgagaca nactagnaana ttcctagtga tggctcanga    360
ttccaaatgg nctcatntcn aatgtttaaa agttanttaa gtgtaagaaa tacagactgg    420
atgttccacc aactagtacc tgtaatgaacn ggccctgtccc aacacatctc ccttttccat    480
gactgtggta nccccgcatcg gaaaaa    506

```

<210> 107

<211> 452

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (452)

<223> n = A,T,C or G

```

<400> 107
gttgagctctg tactaaacag taagatatct caatgaacca taaattcaac tttgtaaaaa    60
tcttttgaag catagataat attgtttgggt aaatgtttct tttgtttgggt aaatgtttct    120
tttaaagacc ctccattctt ataaaactct gcatgtagag gcttgtttac ctttctctct    180
ctaaggttta caataggagt ggtgatttga aaaatataaa attatgagat tgggttttcct    240
gtggcataaa ttgcatcact gtatcatttt cttttttaac cggtaagant ttcagtttgt    300
tggaagtaaa ctgtganaac ccagtttccc gtccatctcc cttagggact acccatagaa    360
catgaaaagg tccccacnga agcaagaaga taagtcttcc atggctgctg gttgcttaaa    420
ccactttaaa accaaaaaat tccccttggg aa    452

```

<210> 108

<211> 502

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (502)

<223> n = A,T,C or G

```

<400> 108
atcttcttcc cttaattagt tnttatttat ntattaaatt ttattgcatg tcctggcaaa    60
caaaaagaga ttgtagattg gcttctgggt ccccaaaagc ccataacaga aagtaccaca    120
agaccncaac tgaagcttaa aaaatctatc acatgtataa tacctttnga agaacattaa    180
tanagcatat aaaactttta acatntgctt aatgttgtnc aattataaaa ntaatngaaa    240
aaaatgtccc tttaacatnc aatatccac atagtgttat ttnaggggat taccnngnaa    300
naaaaaaagg gtagaaggga tttaatgaaa actctgcttn ccatttctgt ttanaaacgt    360
ctccagaaca aaaacttntc aantctttca gctaaccgca tttgagctna ggccactcaa    420
aaactccatt agnccactt tctaanggtc tctanagctt actaanccct ttgacccctt    480
accctggnta ctctgccct ca    502

```

<210> 109

<211> 1308

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 109

```

acccgaggtc tcgctaaaat catcatggat tcaacttggcg ccgtcagcac tcgacttggg      60
tttgatcttt tcaaagagct gaagaaaaca aatgatggca acatcttctt ttcccctgtg      120
ggcatcttga ctgcaattgg catggtctct ctggggaccc gaggagccac cgcttccag      180
ttggaggagg tgtttcactc tgaaaaagag acgaagagct caagaataaa ggctgaagaa      240
aaagaggtga ttgagaacac agaagcagta catcaacaat tccaaaagtt tttgactgaa      300
ataagcaaac tcaactaatga ttatgaactg aacataacca acaggctgtt tggagaaaaa      360
acatacctct tccttcaaaa atacttagat tatgttgaaa aatattatca tgcactctctg      420
gaacctgttg attttgtaaa tgcagccgat gaaagtcgaa agaagattaa ttcttgggtt      480
gaaagcaaaa caaatgaaaa aatcaaggac ttgttcccag atggctctat tagtagctct      540
accaagctgg tgctggtgaa catggtttat tttaaagggc aatgggacag ggagtttaag      600
aaagaaaata ctaaggaaga gaaatttttg atgaataaga gcacaagtaa atctgtacag      660
atgatgacac agagccattc cttagcttc actttcctgg aggacttgca ggccaaaatt      720
ctagggattc catataaaaa caacgacctc agcatgtttg tgcttctgcc caacgacatc      780
gatggcctgg agaagataat agataaaaata agtcctgaga aattggtaga gtggactagt      840
ccagggcata tggaagaaag aaaggtgaat ctgcacttgc cccggtttga ggtggaggac      900
agttacgac tagaggcggg cctggctgcc atggggatgg gcgatgcctt cagtgagcac      960
aaagccgact actcggaat gtcgtcaggc tccgggttgt acgcccagaa gttcctgcac      1020
agttcctttg tggcagtaac tgaggaaggc accgaggctg cagctgccac tggcataggc      1080
tttactgtca catccgcccc aggtcatgaa aatgttact gcaatcatcc cttcctgttc      1140
ttcatcaggc acaatgaatc caacagcatc ctcttcttcg gcagattttc ttctccttaa      1200
gatgatcgtt gccatggcat tgctgctttt agcaaaaaac aactaccagt gttactcata      1260
tgattatgaa aatcgccat tcttttaaat ggtggctcac ttgcattt      1308

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&lt;210&gt; 110

&lt;211&gt; 391

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 110

```

Met Asp Ser Leu Gly Ala Val Ser Thr Arg Leu Gly Phe Asp Leu Phe
 1              5              10              15
Lys Glu Leu Lys Lys Thr Asn Asp Gly Asn Ile Phe Phe Ser Pro Val
 20              25              30
Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
 35              40              45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
 50              55              60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Ile Glu Asn Thr Glu
 65              70              75              80
Ala Val His Gln Gln Phe Gln Lys Phe Leu Thr Glu Ile Ser Lys Leu
 85              90              95
Thr Asn Asp Tyr Glu Leu Asn Ile Thr Asn Arg Leu Phe Gly Glu Lys
100              105              110
Thr Tyr Leu Phe Leu Gln Lys Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr
115              120              125
His Ala Ser Leu Glu Pro Val Asp Phe Val Asn Ala Ala Asp Glu Ser
130              135              140
Arg Lys Lys Ile Asn Ser Trp Val Glu Ser Lys Thr Asn Glu Lys Ile
145              150              155              160
Lys Asp Leu Phe Pro Asp Gly Ser Ile Ser Ser Thr Lys Leu Val
165              170              175

```

Leu Val Asn Met Val Tyr Phe Lys Gly Gln Trp Asp Arg Glu Phe Lys  
 180 185 190  
 Lys Glu Asn Thr Lys Glu Glu Lys Phe Trp Met Asn Lys Ser Thr Ser  
 195 200 205  
 Lys Ser Val Gln Met Met Thr Gln Ser His Ser Phe Ser Phe Thr Phe  
 210 215 220  
 Leu Glu Asp Leu Gln Ala Lys Ile Leu Gly Ile Pro Tyr Lys Asn Asn  
 225 230 235 240  
 Asp Leu Ser Met Phe Val Leu Leu Pro Asn Asp Ile Asp Gly Leu Glu  
 245 250 255  
 Lys Ile Ile Asp Lys Ile Ser Pro Glu Lys Leu Val Glu Trp Thr Ser  
 260 265 270  
 Pro Gly His Met Glu Glu Arg Lys Val Asn Leu His Leu Pro Arg Phe  
 275 280 285  
 Glu Val Glu Asp Ser Tyr Asp Leu Glu Ala Val Leu Ala Ala Met Gly  
 290 295 300  
 Met Gly Asp Ala Phe Ser Glu His Lys Ala Asp Tyr Ser Gly Met Ser  
 305 310 315 320  
 Ser Gly Ser Gly Leu Tyr Ala Gln Lys Phe Leu His Ser Ser Phe Val  
 325 330 335  
 Ala Val Thr Glu Glu Gly Thr Glu Ala Ala Ala Thr Gly Ile Gly  
 340 345 350  
 Phe Thr Val Thr Ser Ala Pro Gly His Glu Asn Val His Cys Asn His  
 355 360 365  
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 Phe Gly Arg Phe Ser Ser Pro  
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&lt;210&gt; 111

&lt;211&gt; 1419

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 111

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&lt;210&gt; 112

&lt;211&gt; 400

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 112

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Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
          35          40          45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
          50          55          60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Val Arg Ile Lys Ala
65          70          75          80
Glu Gly Lys Glu Ile Glu Asn Thr Glu Ala Val His Gln Gln Phe Gln
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Lys Phe Leu Thr Glu Ile Ser Lys Leu Thr Asn Asp Tyr Glu Leu Asn
          100          105          110
Ile Thr Asn Arg Leu Phe Gly Glu Lys Thr Tyr Leu Phe Leu Gln Lys
          115          120          125
Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr His Ala Ser Leu Glu Pro Val
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Asp Phe Val Asn Ala Ala Asp Glu Ser Arg Lys Lys Ile Asn Ser Trp
145          150          155          160
Val Glu Ser Lys Thr Asn Glu Lys Ile Lys Asp Leu Phe Pro Asp Gly
          165          170          175
Ser Ile Ser Ser Ser Thr Lys Leu Val Leu Val Asn Met Val Tyr Phe
          180          185          190
Lys Gly Gln Trp Asp Arg Glu Phe Lys Lys Glu Asn Thr Lys Glu Glu
          195          200          205
Lys Phe Trp Met Asn Lys Ser Thr Ser Lys Ser Val Gln Met Met Thr
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Gln Ser His Ser Phe Ser Phe Thr Phe Leu Glu Asp Leu Gln Ala Lys
225          230          235          240
Ile Leu Gly Ile Pro Tyr Lys Asn Asn Asp Leu Ser Met Phe Val Leu
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Leu Pro Asn Asp Ile Asp Gly Leu Glu Lys Ile Ile Asp Lys Ile Ser
          260          265          270
Pro Glu Lys Leu Val Glu Trp Thr Ser Pro Gly His Met Glu Glu Arg
          275          280          285
Lys Val Asn Leu His Leu Pro Arg Phe Glu Val Glu Asp Ser Tyr Asp
          290          295          300
Leu Glu Ala Val Leu Ala Ala Met Gly Met Gly Asp Ala Phe Ser Glu
305          310          315          320
His Lys Ala Asp Tyr Ser Gly Met Ser Ser Gly Ser Gly Leu Tyr Ala
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Gln Lys Phe Leu His Ser Ser Phe Val Ala Val Thr Glu Glu Gly Thr
          340          345          350

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 <212> PRT  
 <213> Homo sapien

<400> 114  
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 Gly Asn Thr Lys Ile Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro  
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 85 90 95  
 Gly Tyr Thr Lys Val Pro Glu Pro Gly Ser Ile Lys Val Pro Asp Gln  
 100 105 110  
 Gly Phe Ile Lys Phe Pro Glu Pro Gly Ala Ile Lys Val Pro Glu Gln  
 115 120 125  
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Lys

150

155

160

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&lt;210&gt; 117

&lt;211&gt; 6921

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 117

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&lt;213&gt; Homo sapien

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8948

<210> 120  
 <211> 587  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(587)  
 <223> n = A,T,C or G

<400> 120  
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<210> 121  
 <211> 619  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(619)  
 <223> n = A,T,C or G

<400> 121  
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 aatgaagtcc ctggtttttc atggcaactt gatcagtaaa ggattcncct ctggttggtg 540  
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 aagtgggtggg gaaaaaaa 619

<210> 122  
 <211> 1475  
 <212> DNA  
 <213> Homo sapien

<400> 122  
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&lt;210&gt; 123

&lt;211&gt; 2294

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 123

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&lt;210&gt; 124

&lt;211&gt; 956

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 124

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&lt;210&gt; 125

&lt;211&gt; 486

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (486)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 125

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<210> 126

<211> 3552

<212> DNA

<213> Homo sapien

<400> 126

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&lt;210&gt; 127

&lt;211&gt; 754

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 127

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&lt;210&gt; 128

&lt;211&gt; 374

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 128

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&lt;210&gt; 129

&lt;211&gt; 546

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 129

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&lt;210&gt; 130

&lt;211&gt; 5156

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 130

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&lt;210&gt; 135

&lt;211&gt; 2856

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 135

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&lt;210&gt; 136

&lt;211&gt; 356

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 136

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&lt;210&gt; 137

&lt;211&gt; 356

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (356)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 137

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&lt;210&gt; 138

&lt;211&gt; 353

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 138

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&lt;210&gt; 139

&lt;211&gt; 371

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 139

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&lt;210&gt; 140

&lt;211&gt; 370

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 140

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gcacactggc						370

&lt;210&gt; 141

&lt;211&gt; 371

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 141

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&lt;210&gt; 142

&lt;211&gt; 343

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 142

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&lt;210&gt; 143

&lt;211&gt; 354

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 143

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&lt;210&gt; 144

&lt;211&gt; 353

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 144

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&lt;210&gt; 145

&lt;211&gt; 371

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 145

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<210> 146

<211> 355

<212> DNA

<213> Homo sapien

<400> 146

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<210> 147

<211> 355

<212> DNA

<213> Homo sapien

<400> 147

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<210> 148

<211> 369

<212> DNA

<213> Homo sapien

<400> 148

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acttcttca 369

<210> 149

<211> 620

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(620)

<223> n = A,T,C or G

<400> 149

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&lt;210&gt; 150

&lt;211&gt; 371

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 150

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&lt;210&gt; 151

&lt;211&gt; 4655

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 151

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<210> 152  
 <211> 586  
 <212> PRT  
 <213> Homo sapien

<400> 152  
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 20 25 30  
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
 35 40 45  
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
 50 55 60  
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65 70 75 80  
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
 85 90 95  
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
 100 105 110  
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
 115 120 125  
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
 130 135 140  
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
 145 150 155 160  
 Glu Gly Gln Ile Ala Pro Ser Ser His Leu Ile Arg Val Glu Gly Asn  
 165 170 175  
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
 180 185 190  
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
 195 200 205  
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
 210 215 220  
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
 225 230 235 240  
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 245 250 255  
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
 260 265 270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
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 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
 290 295 300  
 Glu Leu Val Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Val Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Leu Gln His  
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 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu  
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 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
 370 375 380

Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
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 405 410 415  
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro  
 420 425 430  
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro  
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 485 490 495  
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln  
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 530 535 540  
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro  
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 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu  
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&lt;210&gt; 153

&lt;211&gt; 2007

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 153

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&lt;210&gt; 154

&lt;211&gt; 2148

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 154

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 <212> PRT  
 <213> Homo sapien

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 35 40 45  
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys  
 50 55 60  
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp  
 65 70 75 80  
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr  
 85 90 95  
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala  
 100 105 110  
 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu  
 115 120 125  
 Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser  
 130 135 140  
 Glu Asn Gln Gly Ala Phe Lys Gly Met  
 145 150

<210> 156  
 <211> 128  
 <212> PRT  
 <213> Homo sapien

<400> 156  
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 35 40 45  
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys  
 50 55 60  
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp  
 65 70 75 80  
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Thr Ile  
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 Cys Ala Ile Asp Asp Gln Lys Thr Val Glu Glu Gly Phe Met Glu Asp  
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<210> 157  
 <211> 424  
 <212> DNA  
 <213> Homo sapien

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<210> 159  
 <211> 291  
 <212> PRT  
 <213> Homo sapien

<400> 159  
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 Val Met Ile Leu Val Val Ala Ala Gln Glu Val Trp Gly Asp Glu Gln  
 35 40 45  
 Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys  
 50 55 60  
 Tyr Asp His Phe Phe Pro Val Ser His Ile Arg Leu Trp Ala Leu Gln  
 65 70 75 80  
 Leu Ile Phe Val Ser Thr Pro Ala Leu Leu Val Ala Met His Val Ala  
 85 90 95  
 Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg  
 100 105 110  
 Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys Gln Lys Val Arg Ile  
 115 120 125  
 Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Ile  
 130 135 140  
 Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly  
 145 150 155 160  
 Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn  
 165 170 175  
 Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr  
 180 185 190  
 Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala  
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 Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg  
 210 215 220  
 Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys  
 225 230 235 240  
 Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile  
 245 250 255  
 Thr Gly Ser Gln Ala Lys His Phe Lys Val Lys Cys Ser Cys Val Ile  
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 Ser Val Ala  
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<210> 160  
 <211> 3951  
 <212> DNA  
 <213> Homo sapien

<400> 160  
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&lt;210&gt; 161

&lt;211&gt; 943

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 161

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Met Thr Gln Arg Ser Ile Ala Gly Pro Ile Cys Asn Leu Lys Phe Val
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20     25     30
Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn
35     40     45
Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
50     55     60
Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
65     70     75     80
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
85     90     95
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
100    105    110
Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
115    120    125
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
130    135    140
Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
145    150    155    160
Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu
165    170    175
Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys
180    185    190
Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys
195    200    205
Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu
210    215    220
Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile
225    230    235    240
Met Phe Met Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser
245    250    255
Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu
260    265    270
Arg Ser Ala Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser
275    280    285
Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu
290    295    300

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Val Glu Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser  
 305 310 315 320  
 Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu  
 325 330 335  
 Phe Tyr Leu Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala  
 340 345 350  
 Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn  
 355 360 365  
 Ser Asn Asp Asp Arg Lys Leu Leu Val Ser Tyr Leu Pro Thr Thr Val  
 370 375 380  
 Ser Ala Lys Thr Asp Ile Ser Ile Cys Ser Gly Leu Lys Lys Gly Phe  
 385 390 395 400  
 Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile  
 405 410 415  
 Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr  
 420 425 430  
 Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser  
 435 440 445  
 Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys  
 450 455 460  
 Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe  
 465 470 475 480  
 Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln  
 485 490 495  
 Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn  
 500 505 510  
 Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val  
 515 520 525  
 Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp  
 530 535 540  
 Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg  
 545 550 555 560  
 Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr  
 565 570 575  
 Tyr Thr Leu Asn Asn Thr His His Ser Leu Gln Ala Leu Lys Val Thr  
 580 585 590  
 Val Thr Ser Arg Ala Ser Asn Ser Ala Val Pro Pro Ala Thr Val Glu  
 595 600 605  
 Ala Phe Val Glu Arg Asp Ser Leu His Phe Pro His Pro Val Met Ile  
 610 615 620  
 Tyr Ala Asn Val Lys Gln Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val  
 625 630 635 640  
 Thr Ala Thr Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu  
 645 650 655  
 Leu Asp Asp Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr  
 660 665 670  
 Ser Arg Tyr Phe Phe Ser Phe Ala Asn Gly Arg Tyr Ser Leu Lys  
 675 680 685  
 Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile  
 690 695 700  
 Pro Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn  
 705 710 715 720  
 Ile Gln Met Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu  
 725 730 735  
 Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val

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<210> 162
<211> 498
<212> DNA
<213> Homo sapien
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<210> 163
<211> 1128
<212> DNA
<213> Homo sapien
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<400> 163							
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gcagatacct aactcaggaa actaacaagg tggagacgta caaagagcag ccgctcaaga 480
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&lt;210&gt; 164

&lt;211&gt; 1310

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 164

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&lt;210&gt; 165

&lt;211&gt; 177

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 165

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Met Gln Arg Arg Leu Val Gln Gln Trp Ser Val Ala Val Phe Leu Leu
 1           5           10          15
Ser Tyr Ala Val Pro Ser Cys Gly Arg Ser Val Glu Gly Leu Ser Arg
          20          25          30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
          35          40          45
Lys Ser Ile Gln Asp Leu Arg Arg Phe Phe Leu His His Leu Ile

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      50      55      60
Ala Glu Ile His Thr Ala Glu Ile Arg Ala Thr Ser Glu Val Ser Pro
65      70      75      80
Asn Ser Lys Pro Ser Pro Asn Thr Lys Asn His Pro Val Arg Phe Gly
      85      90      95
Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
      100      105      110
Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Lys Gly
      115      120      125
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
      130      135      140
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp
145      150      155      160
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg
      165      170      175
His

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<210> 166
<211> 177
<212> PRT
<213> Homo sapien

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      <400> 166
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Ser Tyr Ala Val Pro Ser Cys Gly Arg Ser Val Glu Gly Leu Ser Arg
      20      25      30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
      35      40      45
Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile
      50      55      60
Ala Glu Ile His Thr Ala Glu Ile Arg Ala Thr Ser Glu Val Ser Pro
      65      70      75      80
Asn Ser Lys Pro Ser Pro Asn Thr Lys Asn His Pro Val Arg Phe Gly
      85      90      95
Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
      100      105      110
Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Lys Gly
      115      120      125
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
      130      135      140
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp
145      150      155      160
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg
      165      170      175
His

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<210> 167
<211> 3362
<212> DNA
<213> Homo sapien

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<400> 167

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agaaggatgc	accttttatct	acaatagcac	ccaaaatgca	actgcatcaa	taatgttcat	780
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 <212> DNA  
 <213> Homo sapien

<400> 168

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2784

&lt;210&gt; 169

&lt;211&gt; 592

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 169

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Val	Gln	Leu	Gln	Asp	Asn	Gly	Tyr	Asn	Gly	Leu	Leu	Ile	Ala	Ile	Asn
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Pro	Gln	Val	Pro	Glu	Asn	Gln	Asn	Leu	Ile	Ser	Asn	Ile	Lys	Glu	Met
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Val	Thr	Asp	Trp	Tyr	Gly	Ala	His	Gly	Asp	Asp	Pro	Tyr	Thr	Leu	Gln
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Tyr	Arg	Gly	Cys	Gly	Lys	Glu	Gly	Lys	Tyr	Ile	His	Phe	Thr	Pro	Asn
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Phe	Leu	Leu	Asn	Asp	Asn	Leu	Thr	Ala	Gly	Tyr	Gly	Ser	Arg	Gly	Arg
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Val	Phe	Val	His	Glu	Trp	Ala	His	Leu	Arg	Trp	Gly	Val	Phe	Asp	Glu
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Tyr	Asn	Asn	Asp	Lys	Pro	Phe	Tyr	Ile	Asn	Gly	Gln	Asn	Gln	Ile	Lys
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Val	Thr	Arg	Cys	Ser	Ser	Asp	Ile	Thr	Gly	Ile	Phe	Val	Cys	Glu	Lys
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Val	Glu	Ala	Gly	Asp	Lys	Val	Val	Cys	Leu	Val	Leu	Asp	Val	Ser	Ser
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Lys	Met	Ala	Glu	Ala	Asp	Arg	Leu	Leu	Gln	Leu	Gln	Gln	Ala	Ala	Glu
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Ser	Phe	Asp	Ser	Lys	Gly	Glu	Ile	Arg	Ala	Gln	Leu	His	Gln	Ile	Asn
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Ser	Asn	Asp	Asp	Arg	Lys	Leu	Leu	Val	Ser	Tyr	Leu	Pro	Thr	Thr	Val

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Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr
              420              425              430
Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser
              435              440              445
Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys
              450              455              460
Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
465              470              475              480
Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
              485              490              495
Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
              500              505              510
Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val
              515              520              525
Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp
              530              535              540
Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg
545              550              555              560
Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
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Tyr Thr Leu Met Cys Phe His His Ala Lys Leu Leu Thr Trp Lys Leu
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&lt;210&gt; 170

&lt;211&gt; 791

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 170

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Thr Leu Leu Val Ala Leu Ser Ser Glu Leu Pro Phe Leu Gly Ala Gly
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Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn
              35              40              45
Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
              50              55              60
Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
65              70              75              80
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
              85              90              95
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
              100              105              110
Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
              115              120              125
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
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Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
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Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu

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Ala	Ala	Pro	Asn	Leu	Glu	Glu	Leu	Ser	Arg	Leu	Thr	Gly	Gly	Leu	Lys	
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Ser	Arg	Ile	Ser	Ser	Gly	Thr	Gly	Asp	Ile	Phe	Gln	Gln	His	Ile	Gln	
			485					490						495		
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 625 630 635 640  
 Thr Ala Thr Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu  
 645 650 655  
 Leu Asp Asp Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr  
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 Ser Arg Tyr Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys  
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 Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile  
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 <212> DNA  
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1491

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<211> 364

<212> PRT

<213> Homo sapien

<400> 172

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			20					25					30		
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		35					40					45			
Ser	Pro	Gly	Arg	Pro	Arg	Glu	Leu	Thr	Ile	Pro	Gln	Thr	Ser	Ser	His
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Gly	Ala	Asn	Arg	Phe	Val	Pro	Lys	Ser	Lys	Ala	Leu	Glu	Ala	Val	Lys
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Leu	Ala	Ile	Glu	Ala	Gly	Phe	His	His	Ile	Asp	Ser	Ala	His	Val	Tyr
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Asn	Asn	Glu	Glu	Gln	Val	Gly	Leu	Ala	Ile	Arg	Ser	Lys	Ile	Ala	Asp
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Gly	Ser	Val	Lys	Arg	Glu	Asp	Ile	Phe	Tyr	Thr	Ser	Lys	Leu	Trp	Ser
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	130					135					140				
Lys	Asn	Leu	Gln	Leu	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Phe	Pro
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Val	Ser	Val	Lys	Pro	Gly	Glu	Glu	Val	Ile	Pro	Lys	Asp	Glu	Asn	Gly
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Glu	Lys	Cys	Lys	Asp	Ala	Gly	Leu	Ala	Lys	Ser	Ile	Gly	Val	Ser	Asn
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Phe	Asn	His	Arg	Leu	Leu	Glu	Met	Ile	Leu	Asn	Lys	Pro	Gly	Leu	Lys
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Tyr	Lys	Pro	Val	Cys	Asn	Gln	Val	Glu	Cys	His	Pro	Tyr	Phe	Asn	Gln
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Arg	Lys	Leu	Leu	Asp	Phe	Cys	Lys	Ser	Lys	Asp	Ile	Val	Leu	Val	Ala
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Tyr	Ser	Ala	Leu	Gly	Ser	His	Arg	Glu	Glu	Pro	Trp	Val	Asp	Pro	Asn
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Ser	Pro	Val	Leu	Leu	Glu	Asp	Pro	Val	Leu	Cys	Ala	Leu	Ala	Lys	Lys
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His	Lys	Arg	Thr	Pro	Ala	Leu	Ile	Ala	Leu	Arg	Tyr	Gln	Leu	Gln	Arg
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305				310						315					320
Asn	Val	Gln	Val	Phe	Glu	Phe	Gln	Leu	Thr	Ser	Glu	Glu	Met	Lys	Ala
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Ile	Asp	Gly	Leu	Asn	Arg	Asn	Val	Arg	Tyr	Leu	Thr	Leu	Asp	Ile	Phe
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 <213> Homo sapiens

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Leu Gln Ser Ser Asp His Gly Gln Thr Ser Ser Leu Trp Trp Lys Cys		
85	90	95
Ser Gln Glu Gly Gly Gly Ser Gly Ser Tyr Glu Glu Gly Cys Gln Ser		
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Leu Met Glu Tyr Ala Trp Gly Arg Ala Ala Ala Met Leu Phe Cys		
115	120	125
Gly Phe Ile Ile Leu Val Ile Cys Phe Ile Leu Ser Phe Phe Ala Leu		
130	135	140
Cys Gly Pro Gln Met Leu Val Phe Leu Arg Val Ile Gly Gly Leu Leu		
145	150	155 160
Ala Leu Ala Ala Val Phe Gln Ile Ile Ser Leu Val Ile Tyr Pro Val		
165	170	175
Lys Tyr Thr Gln Thr Phe Thr Leu His Ala Asn Pro Ala Val Thr Tyr		
180	185	190
Ile Tyr Asn Trp Ala Tyr Gly Phe Gly Trp Ala Ala Thr Ile Ile Leu		
195	200	205
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4181

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<211> 580

<212> PRT

<213> Homo sapiens

<400> 176

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Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser  
35 40 45

Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His  
50 55 60

Gly Lys Pro Ile Glu Val Glu His Ser Val Pro Lys Arg Gln Arg Ile  
65 70 75 80

Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val  
85 90 95

Leu Asp Ser Leu Leu Val Gln Tyr Gly Val Val Glu Ser Cys Glu Gln  
100 105 110

Val	Asn	Thr	Asp	Ser	Glu	Thr	Ala	Val	Val	Asn	Val	Thr	Tyr	Ser	Ser
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Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu  
130 135 140

Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Met Ala Ala  
145 150 155 160

Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly Gln  
165 170 175

Arg Gly Ser Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys  
180 185 190

Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln Phe Val Gly  
195 200 205

Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln  
210 215 220

Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala  
225 230 235 240

Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala  
245 250 255

Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys  
 260 265 270  
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 275 280 285  
 Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln  
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 Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu  
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 Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys  
 325 330 335  
 Ala Lys Ala Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu  
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 385 390 395 400  
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 405 410 415  
 Val Gly Ala Ile Ile Gly Lys Gln Gly Gln His Ile Lys Gln Leu Ser  
 420 425 430  
 Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp  
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 450 455 460  
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 465 470 475 480  
 Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser  
 485 490 495  
 Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu  
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 Leu Gln Asn Leu Ser Ser Ala Glu Val Val Val Pro Arg Asp Gln Thr  
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 Pro Asp Glu Asn Asp Gln Val Val Lys Ile Thr Gly His Phe Tyr  
 530 535 540

Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val  
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Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser  
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<210> 177

<211> 401

<212> DNA

<213> Homo sapiens

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<210> 178

<211> 561

<212> DNA

<213> Homo sapiens

<400> 178

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<211> 521

<212> DNA

<213> Homo sapiens

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<210> 181  
 <211> 283  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> (35)  
 <223> n=A,T,C or G

<400> 181  
 gatttcttct aaataggatg taaaacttct ttcantattac tcttctcag tcctgcctgc 60  
 caagaactca agtgtaactg tgataaaata acctttccca ggtatatggg caggatattg 120  
 tgtaattctca gaatacacag gtgacataga tatgatatga caactggtaa tgggtggattc 180  
 atttacattg tttacacttc tatgaccagg ccttaaggga aggtcagttt tttaaaaaac 240  
 caagtagtgt ctctctacct atctccagat acatgtcaaa aaa 283

<210> 182  
 <211> 401  
 <212> DNA  
 <213> Homo sapiens

<400> 182  
 atattcttgc tgettattgca gctgacattg ttgccctccc taaagcaacc aagtagcctt 60  
 tatttcccac agtgaaagaa aacgctggcc tatcagttac attacaaaag gcagatttca 120  
 agaggattga gtaagtagtt ggatggcttt cataaaaaca agaattcaag aagaggattc 180  
 atgctttaag aaacatttct tatacattcc tcacaaatta tacctgggat aaaaactatg 240  
 tagcaggcag tgtgttttcc ttccatgtct ctctgcacta cctgcagtgt gtcctctgag 300  
 gctgcaagtc tgcctatct gaattcccag cagaagcact aagaagctcc accctatcac 360  
 ctagcagata aaactatggg gaaaacttaa atctgtgcat a 401

<210> 183  
 <211> 366  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> (325)

<223> n=A,T,C or G

<400> 183

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accgtgtcca agttttttaga acccttggtta gccagaccga ggtgtcctgg tcaccgtttc 60
accatcatgc tttgatgttc cctgtctttt ctctcttctg ctctcaagag caaagggttaa 120
tttaaggaca aagatgaagt cactgtaaac taatctgtca ttgtttttac cttccttttc 180
tttttcagtg cagaaattaa aagtaagtat aaagcaccgt gattgggagt gtttttgctg 240
gtgtcggaat cactggtaaa tgttggtga gaacaatccc tccccttgca cttgtgaaaa 300
cactttgagc gctttaagag attancctga gaaataatta aatatctttt ctcttcaaaa 360
aaaaaa 366
```

<210> 184

<211> 370

<212> DNA

<213> Homo sapiens

<400> 184

```
tcttacttca aaagaaaaat aaacataaaa aataagttgc tggttcctaa caggaaaaat 60
tttaataatt gtactgagag aaactgctta cgtacacatt gcagatcaaa tatttgaggt 120
taaaatgtta gtctacatag atgggtgatt gtaactttat tgccattaaa agatttcaaa 180
ttgcattcat gcttctgtgt acacataatg aaaaatgggc aaataatgaa gatctctcct 240
tcagtctgct ctgtttaatt ctgctgtctg ctcttctcta atgctgcgtc cctaattgta 300
cacagtttag tgatatctag gagtataaag ttgtcgccca tcaataaaaa tcacaaagtt 360
ggtttaaaaa 370
```

<210> 185

<211> 107

<212> DNA

<213> Homo sapiens

<400> 185

```
ctcatattat tttccttttg agaaattgga aactctttct gttgctatta tattaataaa 60
gttggtgttt attttctggt agtcaccttc cccatttaa aaaaaa 107
```

<210> 186

<211> 309

<212> DNA

<213> Homo sapiens

<400> 186

```
gaaaggatgg ctctgggttg cacagagctg ggacttcatg ttcttctaga gagggccaca 60
agagggccac aggggtggcc gggagtgtgc agctgatgcc tgctgagagg caggaattgt 120
gccagtgagt gacagtcag agggagtgtc tcttcttggg gaggaaagaa ggtagagcct 180
ttctgtctga atgaaaggcc aaggctacag tacagggccc cgccccagcc aggggtgtta 240
tgcccacgta gtggaggcct ctggcagatc ctgcattcca aggtcactgg actgtacgtt 300
tttatggtt 309
```

<210> 187

<211> 477

<212> DNA

<213> Homo sapiens

<400> 187

```
ttcagtccca gcaagaagcg agaattctga gatcctccag aaagtcgagc agcaccacc 60
tccaacctcg ggccagtgtc ttcaggcttt actggggacc tgcgagctgg cctaattgtg 120
```

tggcctgcaa gccaggccat ccctggggcg cacagacgag ctccgagcca ggtcaggctt 180  
cggaggccac aagctcagcc tcaggcccag gcactgattg tggcagaggg gccactaccc 240  
aaggtctagc taggcccag acctagttag ccagacagtg agaagcccct ggaaggcaga 300  
aaagtggga gcatggcaga cagggaaggg aaacattttc agggaaaaga catgtatcac 360  
atgtcttcag aagcaagtca ggtttcatgt aaccgagtgt cctcttgctg gtccaaaagt 420  
agcccgaggc ttagcacag gtttcacagt gattttgtgt tcagccgtga gtcacac 477

<210> 188

<211> 220

<212> DNA

<213> Homo sapiens

<400> 188

taaatatggg agatattaat attcctctta gatgaccagt gattccaatt gtcccaagtt 60  
ttaaataagt accctgtgag tatgagataa attagtgaac atcagaacaa gtttcagtat 120  
cagatgttca agaggaagtt gctattgcat tgattttaat atttgtacat aaacactgat 180  
ttttttgagc attattttgt atttgttgta ctttaataacc 220

<210> 189

<211> 417

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (76)

<223> n=A,T,C or G

<221> unsure

<222> (77)

<223> n=A,T,C or G

<400> 189

accatcttga cagaggatac atgctcccaa aacgtttgtt accacactta aaaatcactg 60  
ccatcattaa gcacnnttt caaaattata gccattcatg atttactttt tccagatgac 120  
tatcattatt ctagtccctt gaattttgtaa ggggaaaaaa aacaaaaaca aaaacttacg 180  
atgcactttt ctccagcaca tcagatttca aattgaaaat taaagacatg ctatggtaat 240  
gcacttgcta gtactacaca ctttgtacaa caaaaaacag aggcaagaaa caacggaaaag 300  
agaaaagcct tcctttgttg gcccttaaac tgagtcaaga tctgaaatgt agagatgatc 360  
tctgacgata cctgtatgtt cttattgtgt aaataaaaatt gctgggtatga aatgaca 417

<210> 190

<211> 497

<212> DNA

<213> Homo sapiens

<400> 190

gcactggggc gctctcccgt cccgcggttg ttgctgctgc tgccgctgct gctgggcttg 60  
aacgcaggag ctgtcattga ctggcccaca gaggagggca aggaagtatg ggattatgtg 120  
acggtccgca aggatgccta catgttcttg tggctctatt atgccacca ctctgcaag 180  
aacttctcag aactgcccct ggcatgttg cttcagggcg gtccaggcgg ttctagcact 240  
ggatttgga actttgagga aattgggccc cttgacagt atctcaaacc acggaaaacc 300  
acctggctcc aggtgcccag tctctattt gtggataatc ccgtgggcac tgggttcagt 360  
tatgtgaatg gtagtggtgc ctatgccaag gacctggcta tgggtggctt agacatgatg 420  
gttctcctga agaccttctt cagttgccac aaagaattcc agacagttcc attctacatt 480  
ttctcagagt cctatggg 497

<210> 191  
<211> 175  
<212> DNA  
<213> Homo sapiens

<400> 191  
atgttgaata ttttgcttat taactttggt tattgtcttc tccctcgatt agaattattag 60  
ctacttgagt acaaggattt gagcctgtta cattcactgc tgaatttttag gtccttgga 120  
gataccagc attcaataga gaccacacaa taaatatatg tcaaataaaa aaaaa 175

<210> 192  
<211> 526  
<212> DNA  
<213> Homo sapiens

<400> 192  
agtaaacatt attatTTTTT ttatatTTTgc aaaggaaaca tatctaattcc ttcctataga 60  
aagaacagta ttgctgtaat tccttttctt ttcttctca ttcctctgc ccctaaaag 120  
attgaagaaa gagaaacttg tcaactcata tccacgttat ctacaaagt acataagaat 180  
ctatcactaa gtaatgtatc cttcagaatg tgttggttta ccagtgcac cccatattca 240  
tcacaaaatt aaagcaagaa gtccatagta atttatttgc taatagtga tttttaatgc 300  
tcagagtttc tgagggtcaaa ttttatcttt tcacttacia gctctatgat cttaaataat 360  
ttacttaatg tattttggtg tattttcttc aaattaatat tgggtgttcaa gactatatct 420  
aattcctctg atcactttga gaaacaaact tttattaaat gtaaggcact tttctatga 480  
ttttaaatat aaaaataaat attgttctga ttattactga aaaaaa 526

<210> 193  
<211> 553  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> (290)  
<223> n=A,T,C or G  
<221> unsure  
<222> (300)  
<223> n=A,T,C or G  
<221> unsure  
<222> (411)  
<223> n=A,T,C or G  
<221> unsure  
<222> (441)  
<223> n=A,T,C or G

<400> 193  
tcattgtgg tggaattcgc tctctggtaa aggcgtgcag gtgttgccg cgccctctga 60  
gctgggatga gccgtgctcc cgggtggaagc aaggagccc agccggagcc atggccagta 120  
cagtggtagc agttggactg accattgctg ctgcaggatt tgcaggccgt tacgttttgc 180  
aagccatgaa gcatatggag cctcaagtaa aacaagtttt tcaaagccta ccaaaatctg 240  
ccttcagtgg tggctattat agaggtgggt ttgaacccaa aatgacaaan cggaagcan 300  
cattaatact aggtgtaagc cctactgcca ataaagggaa aataagagat gctcatcgac 360  
gaattatgct tttaaatcat cctgacaaag gaggatctcc ttatatagca nccaaaatca 420  
atgaagctaa agatttacta naaggtcaag ctaaaaaatg aagtaaattg atgatgaatt 480

ttaagttcgt attagtttat gtatatgagt actaagtttt tataataaaa tgcctcagag 540  
ctacaattttt aaa 553

<210> 194  
<211> 320  
<212> DNA  
<213> Homo sapiens

<400> 194  
cccttcccaa tccatcagta aagaccccat ctgccttgtc catgccgttt cccaacaggg 60  
atgtcacttg atatgagaat ctcaaatttc aatgccttat aagcattcct tcctgtgtcc 120  
attaagactc tgataattgt ctccctccca taggaatttc tcccaggaaa gaaatatatc 180  
cccattctcg ttcatatca gaactaccgt ccccgatatt cccttcagag agattaaaga 240  
ccagaaaaaa gtgagcctct tcatctgcac ctgtaatagt ttcagttcct attttcttcc 300  
attgacccat atttatacct 320

<210> 195  
<211> 320  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> (203)  
<223> n=A,T,C or G  
<221> unsure  
<222> (218)  
<223> n=A,T,C or G

<400> 195  
aagcatgacc tggggaaatg gtcagacctt gtattgtggt tttggccttg aaagtagcaa 60  
gtgaccagaa tctgccatgg caacaggctt taaaaaagac ccttaaaaag acactgtctc 120  
aactgtggtg ttagcaccag ccagctctct gtacatttgc tagcttgtag ttttctaaga 180  
ctgagtaaac ttcttatttt tanaaagggg aggctggntt gtaactttcc ttgtacttaa 240  
ttgggtaaaa gtcttttcca caaaccacca tctattttgt gaactttggt agtcatcttt 300  
tatttggtaa attatgaact 320

<210> 196  
<211> 357  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> (36)  
<223> n=A,T,C or G

<400> 196  
atataaaata atacgaaact ttaaaaagca ttggantgtc agtatgttga atcagtagtt 60  
tcactttaac tgtaacaat ttcttaggac accatttggg ctagtctctg tgtaagtgtg 120  
aatactacaa aaacttattt atactgttct tatgtcattt gttatattca tagatttata 180  
tgatgatatg acatctggct aaaaagaaat tattgcaaaa ctaaccacta tgtacttttt 240  
tataaatact gtatggacaa aaaatggcat tttttatatt aaattgttta gctctggcaa 300  
aaaaaaaaa ttttaagagc tgggtactaat aaaggattat tatgactggt aaaaaaa 357

<210> 197  
<211> 565  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> (27)  
<223> n=A,T,C or G

<400> 197  
tcagctgagt accatcagga tatttanccc ttttaagtgt gttttgggag tagaaaaacta 60  
aagcaacaat acttcctctt gacagctttg attggaatgg gggtattaga tcattcacct 120  
tggtcctaca ctttttagga tgcttggtga acataacacc acttataatg aacatccctg 180  
gttcctatat tttgggctat gtgggtagga attgttactt gttactgcag cagcagccct 240  
agaaagtaag ccaggggctt cagatctaag ttagtccaaa agctaaatga tttaaagtca 300  
agttgtaatg ctaggcataa gcaactctata atacattaaa ttataggccg agcaattagg 360  
gaatgtttct gaaacattaa acttgtattt atgtcactaa aattctaaca caaacttaaa 420  
aaatgtgtct catacatatg ctgtactagg cttcatcatg catttctaaa tttgtgtatg 480  
atgtgaatat atgaaagaat ttatacaaga gtgttattta aaattattaa aaataaatgt 540  
atataatttg tacctattgt aaaaa 565

<210> 198  
<211> 484  
<212> DNA  
<213> Homo sapiens

<400> 198  
tatgtaagta ttggtgtctg ctttaaaaaa ggagaccag acttcacctg tccttttta 60  
acatttgaga acagtgttac tctgagcagt tgggccacct tcaccttacc cgacagctga 120  
ctgttggatg tgtccattgt cgccagtttg gctgttgccc ggacaggaca ggacctccat 180  
tgggcgagc agcaggtggc aggggtgttg cttgaggtgg gtggcagcgt ctggtcctcc 240  
tctctggtgc tttctgagag ggtctctaaa gcagagtgtg gttggcctgg gggaaggcag 300  
agcagctatt tctccctct agtacctctg ctttgtgag tgttccctct ggctttctga 360  
agggcagcag actcttgagt atactgcaga ggacatgctt tatcagtagg tcctgagggc 420  
tccaggggct caactgacca agtaacacag aagttggggg atgtggccta tttgggtcgg 480  
aaac 484

<210> 199  
<211> 429  
<212> DNA  
<213> Homo sapiens

<220>  
<221> unsure  
<222> (77)  
<223> n=A,T,C or G  
<221> unsure  
<222> (88)  
<223> n=A,T,C or G  
<221> unsure  
<222> (134)  
<223> n=A,T,C or G  
<221> unsure  
<222> (151)

<223> n=A,T,C or G  
 <221> unsure  
 <222> (189)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (227)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (274)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (319)  
 <223> n=A,T,C or G

<400> 199  
 gcttatgttt tttgttttaa cttttgtttt ttaacattta gaatattaca ttttgtatta 60  
 tacagtacct ttctcanaca ttttgtanaa ttcatttcgg cagctcacta ggattttgct 120  
 gaacattaaa aagngtgata gcgatattag ngccaatcaa atggaaaaaa ggtagtctta 180  
 ataaacaana cacaacgttt ttatacaaca tactttaaaa tattaanaaa actccttaat 240  
 attgtttcct attaagtatt attctttggg caanattttc tgatgctttt gatttttctt 300  
 caatttagca tttgctttng gtttttttct ctatttagca ttctgttaag gcacaaaaac 360  
 tatgtactgt atgggaaatg ttgtaaatat taccttttcc acattttaaa cagacaactt 420  
 tgaatccaa 429

<210> 200  
 <211> 279  
 <212> DNA  
 <213> Homo sapiens

<400> 200  
 gcttttttga ggaattacag ggaagctcct ggaattgtac atggatatct ttatccctag 60  
 ggggaaatca aggagctggg caccctaat tctttatgga agtgtttaaa actattttta 120  
 ttttattaca agtattacta gagtagtggt tctactctaa gattttcaaaa gtgcatttaa 180  
 aatcatacat gttccgcgct gcaaatatat tgttattttg gtggagaaaa aaatagtata 240  
 ttctacataa aaaattaaag atattaacta agaaaaaaa 279

<210> 201  
 <211> 569  
 <212> DNA  
 <213> Homo sapiens

<400> 201  
 taggtcagta tttttagaaa ctcttaatag ctcatactct tgataccaaa agcagccctg 60  
 attgttaaag cacacacctg cacaagaagc agtgatgggt gcattttacat ttcctgggtg 120  
 cacaaaaaaa aattctcaaa aagcaaggac ttacgctttt tgcaaagcct ttgagaagtt 180  
 actggatcat aggaagctta taacaagaat ggaagattct taaataactc actttctttg 240  
 gtatccagta acagtagatg ttcaaaatat gtagctgatt aataccagca ttgtgaacgc 300  
 tgtacaacct tgtggttatt actaagcaag ttactactag cttctgaaaa gtagcttcat 360  
 aattaatggt atttatacac tgccttccat gacttttact ttgccctaag ctaatctcca 420  
 aaatctgaaa tgctactcca atatcagaaa aaaaggggga ggtggaatta tatttctctg 480  
 gattttaaga gtacagagaa tcatgcacat ctctgattag ttcatatatg tctagtgtgt 540  
 aataaaagtc aaagatgaac tctcaaaaa 569

<210> 202  
 <211> 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 202

```
attaataggc ttaataattg ttggcaagga tccttttgct ttctttggca tgcaagctcc 60
tagcatctgg cagtggggcc aagaaaataa ggtttatgca tgtatgatgg ttttcttctt 120
gagcaacatg attgagaacc agtgtatgtc aacagggtgca tttgagataa ctttaaataga 180
tgtacctgtg tggctctaagc tggaaatctgg tcaccttcca tccatgcaac aacttggtca 240
aattcttgac aatgaaatga agctcaatgt gcatatggat tcaatcccac accatcgatc 300
atagcaccac ctatcagcac tgaaaactct tttgcattaa gggatcattg caagagcagc 360
gtgactgaca ttatgaaggc ctgtactgaa gacagcaagc tgtagtaca gaccagatgc 420
tttcttggca ggctcgttgt acctcttgga aaacctcaat gcaagatagt gtttcagtgc 480
tgccatattt tgggaattctg c 501
```

&lt;210&gt; 203

&lt;211&gt; 261

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (36)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (96)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 203

```
gacaagctcc tggctcttgag atgtcttctc gtttaangaga tgggcctttt ggaggttaaag 60
gataaaaatga atgagttctg tcatgattca ctattntata acttgcatac cctttactgt 120
gttagctctt tgaatgttct tgaaatttta gactttcttt gtaaacaat gatatgtcct 180
tatcattgta taaaagctgt tatgtgcaac agtgtggaga ttccttgtct gatttaataa 240
aataacttaa cactgaaaaa a 261
```

&lt;210&gt; 204

&lt;211&gt; 421

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 204

```
agcatctttt ctacaacggt aaaattgcag aagtagctta tcattaaaaa acaacaacaa 60
caacaataac aataaatcct aagtgtaat cagttattct accccctacc aaggatatca 120
gcctgttttt tccctttttt ctctgggaa taattgtggg ctcttccca aatttctaca 180
gcctctttcc tcttctcatg cttgagcttc cctgtttgca cgcagcgtg tgcaggactg 240
gcttgtgtgc ttggactcgg ctccagggtg aagcatgctt tcccttggtta ctgttgga 300
aactcaaac ttcaagccct aggtgtagcc attttgtcaa gtcacaaact gtatttttgt 360
actggcatta acaaaaaaag aagataaat attgtacat taaacttta taaaacttta 420
a 421
```

&lt;210&gt; 205

&lt;211&gt; 460

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 205



```
tactctcaca atgaaggacc tggaaatgaaa aatctgtgtc taaacaagtc ctcttttagat 60
tttagtgcaa atccagagacc agcgtcgggt gcctcgagta attctttcat gggtagcttt 120
ggaaaagctc tcaggagacc tcacctagat gcctattcaa gctttggaca gccatcagat 180
tgtcagccaa gagcctttta tttgaaaagct cattcttccc cagacttgga ctctgggtca 240
gaggaagatg ggaaagaaaag gacagatttt caggaagaaa atcacatttg tacctttaaa 300
cagacttttag aaaactacag gactccaaat tttcagtcct atgacttgga cacatagact 360
gaatgagacc aaaggaaaag cttaacatac tacctcaagg tgaactttta tttaaaagag 420
agagaatctt atgtttttta aatggagtta tgaattttta 460
```

&lt;210&gt; 206

&lt;211&gt; 481

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 206

```
tgtggtggaa ttcggaacgc cccagacccc tgactttttc ctgcgtgggc cgtctcctcc 60
tgcggaagca gtgacctctg acccctgggt accttcgctt tgagtgcctt ttgaacgctg 120
gtcccgcggt acttggtttt ctcaagctct gtctgtccaa agacgctccg gtcgaggtcc 180
cgctggcctt ggggtgatac ttgaacccca gacgcccctc tgtgctgctg tgtccggagg 240
cgcccttccc atctgcctgc ccaccggag ctctttccgc cggcgagggg tcccaagccc 300
acctcccgcc ctgagtcctg cgggtgtcgt ctgggcacgt cctgcacaca caatgcaagt 360
cctggcctcc gcgcccgcgc gccacgcga gccgtaccgc ccgccaactc tgttatttat 420
gggtgtgaccc cctggagggtg ccctcggccc accggggcta tttattgttt aatttatttg 480
t 481
```

&lt;210&gt; 207

&lt;211&gt; 605

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 207

```
accctttttg gattcagggc tcttcacaaat taaaatgagt gtaatgaaac aaggtgaaaa 60
tatagaagca tccctttgta tactgttttg ctacttacag tgtacttggc attgctttat 120
ctcactggat tctcacggta ggatttctga gatcttaata taagctccaa agttgtctac 180
ttttttgatc ctaggggtgt ctttttgttt tacagagcag ggtcacttga tttgctagct 240
gggtggcagaa ttggcaccat taccaggtc tgactgacca ccagtcagag gcactttatt 300
tgtatcatga aatgatttga aatcatttga aagcagcgaa gtctgataat gaatgccagc 360
tttccttggtg ctttgataac aaagactcca aatattctgg agaacctgga taaaagtttg 420
aagggctaga ttgggatttg aagacaaaat ttaggaaat cttacatttt tgcaataaca 480
aacattaatg aaagcaaaac attataaaag taattttaat tcaccacata cttatcaatt 540
tcttgatgct tccaaatgac atctaccaga tatggttttg tggacatctt tttctgttta 600
cataa 605
```

&lt;210&gt; 208

&lt;211&gt; 655

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 208

```
ggcgttgttc tggattcccg tcgtaactta aagggaaact ttcacaatgt ccggagccct 60
tgatgtcctg caaatgaagg aggaggatgt ccttaagttc cttgcagcag gaacccactt 120
aggtggcacc aatcttgact tccagatgga acagtacatc tataaaagga aaagtgatgg 180
catctatatc ataaatctca agaggacctg ggagaagctt ctgctggcag ctctgcaat 240
tgttgccatt gaaaacctg ctgatgtcag tgttatatcc tccaggaata ctggccagag 300
ggctgtgctg aagtttctg ctgccactgg agccactcca attgctggcc gcttcaactc 360
```

```

tggaaccttc actaaccaga tccaggcagc cttccgggag ccacggcttc ttgtgggttac 420
tgacccacagg gctgaccacc agcctctcac ggaggcatct tatgttaacc tacctacat 480
tgcgctgtgt aacacagatt ctctctgcg ctatgtggac attgccatcc catgcaacaa 540
caaggagct cactcagtgg gtttgatgtg gtggatgctg gctcgggaag ttctgcgcat 600
gcgtggcacc atttcccggtg aacacccatg ggaggatcatg cctgatctgt acttc 655

```

&lt;210&gt; 209

&lt;211&gt; 621

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 209

```

catttagaac atggttatca tccaagacta ctctaccctg caacattgaa ctcccaagag 60
caaatccaca ttctcttga gttctgcagc ttctgtgtaa atagggcagc tgcgtctat 120
gccgtagaat cacatgatct gaggaccatt catggaagct gctaaatagc ctagtctggg 180
gagtcttcca taaagttttg catggagcaa acaaacagga ttaactagg tttggttct 240
tcagccctct aaaagcatag ggcttagcct gcaggcttcc ttgggcttcc tctgtgtgtg 300
tagttttgta aacactatag catctgttaa gatccagtgt ccatggaaac cttcccat 360
gccgtgactc tggactatat cagtttttgg aaagcagggt tcctctgcct gctaacaagc 420
ccacgtggac cagtctgaat gtctttcctt tacacctatg tttttaata gtcaaaactc 480
aagaaacaat ctaaacaggt ttctgttgca tatgtgtttg tgaacttgta tttgtattta 540
gtaggcttct atattgcatt taactgttt ttgtaactcc tgattcttcc ttttcggata 600
ctattgatga ataaagaaat t 621

```

&lt;210&gt; 210

&lt;211&gt; 533

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (20)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (21)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (61)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 210

```

cgccttgggg agccggcggn ngagtccggg acgtggagac ccgggggtccc ggcagccggg 60
nggcccgcgg gccaggggtg gggatgcacc gccgcggggg gggagctggc gccatcgcca 120
agaagaaact tgcagaggcc aagtataagg agcgaggagc ggtcttggct gaggaccagc 180
tagcccagat gtcaaagcag ttggacatgt tcaagaccaa cctggaggaa tttgccagca 240
aacacaagca ggagatccgg aagaatcctg agttccgtgt gcagttccag gacatgtgtg 300
caaccattgg cgtggatccg ctggcctctg gaaaaggatt ttggtctgag atgtggggcg 360
tgggggactt ctattacgaa ctagggtgc aaattatcga agtgtgcctg gcgctgaagc 420
atcggaatgg aggtctgata actttggagg aactacatca acaggtgttg aagggaaggg 480
gcaagttcgc ccaggatgtc agtcaagatg acctgatcag agccatcaag aaa 533

```

&lt;210&gt; 211

&lt;211&gt; 451

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 211

```

ttagcttgag ccgagaacga ggcgagaaag ctggagaccg aggagaccgc ctagagcgga 60
gtgaacgggg aggggaccgt ggggaccggc ttgatcgtgc gcggacacct gctaccaagc 120
ggagcttcag caaggaagtg gaggagcgga gtagagaacg gccctcccag cctgaggggc 180
tgcgcaaggc agctagcctc acggaggatc gggaccgtgg gcgggatgcc gtgaagcgag 240
aagctgccct acccccagtg agccccctga aggcggctct ctctgaggag gagttagaga 300
agaaatccaa ggctatcatt gaggaatatc tccatctcaa tgacatgaaa gaggcagtcc 360
agtgcgtgca ggagctggcc tcaccctcct tgctcttcat ctttgtagcg catgggtgcg 420
agtctacgct ggagcgcagt gccattgctc g                                     451

```

&lt;210&gt; 212

&lt;211&gt; 471

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (54)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 212

```

gtgattattc ttgatcaggg agaagatcat ttagatttgt tttgcattcc ttanaatgga 60
gggcaacatt ccacagctgc cctggctgtg atgagtgtcc ttgcaggggc eggagtagga 120
gcactggggg gggggcgga ttggggttac tcgatgtaag ggattccttg ttgttgtgtt 180
gagatccagt gcagtttgtga tttctgtgga tcccagcttg gttccaggaa ttttgtgtga 240
ttggcttaaa tccagttttc aatcttcgac agctgggctg gaacgtgaac tcagtagctg 300
aacctgtctg acccggtcac gttcttggat cctcagaact ctttgctctt gtcgggggtg 360
gggtgggaac tcacgtgggg agcgggtggc gagaaaatgt aaggattctg gaatacatat 420
tccatgggac tttccttccc tctcctgctt cctcttttcc tgctccctaa c                                     471

```

&lt;210&gt; 213

&lt;211&gt; 511

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (27)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (63)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (337)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (442)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 213

```

ctaattagaa acttgctgta cttttntttt tcttttaggg gtcaaggacc ctctttatag 60
ctnccatttg cctacaataa attattgcag cagtttgcaa tactaaaata ttttttatag 120
actttatatt tttccttttg ataaagggat gctgcatagt agagttggtg taattaaact 180
atctcagcgg tttccctgct ttcccttctg ctccatatgc ctcatgtcc ttccaggag 240

```

```

ctcttttaaat cttaaagtgc tacatttcat gctcttagtc aaattctggt accttttttaa 300
taactcttcc cactgcatat ttccatcttg aattggnggt tctaaattct gaaactgtag 360
ttgagataca gctattttaat atttctggga gatgtgcac cctcttcttt gtggttgccc 420
aagggtggtt tgcgtaactg anactccttg atatgcttca gagaatttag gcaaactg 480
gccatggccg tgggagtact gggagtaaaa t 511

```

<210> 214  
 <211> 521  
 <212> DNA  
 <213> Homo sapiens

```

<400> 214
agcattgcc aataatccct aattttccac taaaaatata atgaaatgat gttaagcttt 60
ttgaaaagtt taggttaaac ctactgttgt tagattaatg tatttggtgc ttccctttat 120
ctggaatgtg gcattagctt ttttatttta accctcttta attctattc aattccatga 180
cttaaggttg gagagctaaa cactgggatt tttggataac agactgacag ttttgcataa 240
ttataatcgg cattgtacat agaaaggata tggctacctt ttgttaaate tgcactttct 300
aaatatcaaa aaaggggaaat gaagtataaa tcaatttttg tataatctgt ttgaaacatg 360
agttttatctt gcttaatat agggctttgc cccttttctg taagtctctt gggatcctgt 420
gtagaagctg ttctcattaa acaccaaaca gttaagtcca ttctctggta ctagctacaa 480
attcggttct atattctact taacaattta aataaactga a 521

```

<210> 215  
 <211> 381  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> unsure  
 <222> (17)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (20)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (60)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (61)  
 <223> n=A,T,C or G  
 <221> unsure  
 <222> (365)  
 <223> n=A,T,C or G

```

<400> 215
gagcggagag cggaccngtn agagccctga gcagccccac cgccgcccgc ggcctagttt 60
ncatcacacc ccgggaggag ccgcagctgc cgcagccggc cccagtcacc atcacgcaa 120
ccatgagcag cgaggccgag acccagcagc cgcccgcgc ccccccgcc gcccccgccc 180
tcagcgccgc cgacaccaag cccggcacta cgggcagcgg cgcaggagc ggtggcccgg 240
gcggcctcac atcggcgggc cctgccggcg gggacaagaa ggtcatcgca acgaaggttt 300
tgggaacagt aaaatgggtc aatgtaagga acggatatgg tttcatcaac aggaatgaca 360
ccaangaaga tgtatttgta c 381

```

<210> 216  
 <211> 425

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 216

```
ttactaacta ggtcattcaa ggaagtcaag ttaacttaaa catgtcacct aaatgcactt 60
gatgggtgttg aaatgtccac cttcttaaat ttttaagatg aacttagttc taaagaagat 120
aacaggccaa tcctgaaggt actccctggt tgctgcagaa tgtcagatat tttggatgtt 180
gcataagagt cctatttgcc ccagttaatt caacttttgt ctgcctgttt tgtggactgg 240
ctggctctgt tagaactctg tccaaaaagt gcatggaata taacttgtaa agcttccac 300
aattgacaat atatatgcat gtgtttaaac caaatccaga aagcttaaac aatagagctg 360
cataatagta tttattaaag aatcacaact gtaaacatga gaataactta aggattctag 420
ttagg                                           425
```

&lt;210&gt; 217

&lt;211&gt; 181

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 217

```
gagaaaccaa atgatagggt gtagagcctg atgactccaa acaaagccat caccgcatt 60
cttcctcctt cttctggtgc tacagctcca agggcccttc accttcattg ctgaaatgga 120
actttggctt tttcagtggg agaatatgtt gaagggttca ttttgttcta gaaaaaaaaa 180
a                                           181
```

&lt;210&gt; 218

&lt;211&gt; 405

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 218

```
caggccttcc agttcactga caaacatggg gaagtgtgcc cagctggctg gaaacctggc 60
agtgatacca tcaagcctga tgtccaaaag agcaaagaat atttctccaa gcagaagtga 120
gcgctgggct gttagtagtc caggctgcgg tgggcagcca tgagaacaaa acctcttctg 180
tatttttttt ttccattagt aaaacacaag acttcagatt cagccgaatt gtggtgtctt 240
acaaggcagg cctttcctac agggggtgga gagaccagcc tttcttcctt tggtaggaat 300
ggcctgagtt ggcgttgttg gcaggctact ggtttgtatg atgtattagt agagcaacct 360
attaatcttt tgtagtttgt attaaacttg aactgagaaa aaaaaa                    405
```

&lt;210&gt; 219

&lt;211&gt; 216

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (207)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (210)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 219

```
actccaagag ttagggcagc agagtggagc gatttagaaa gaacatttta aaacaatcag 60
ttaatttacc atgtaaaatt gctgtaaatg ataatgtgta cagattttct gttcaaatat 120
tcaattgtaa acttcttgtt aagactgtta cgtttctatt gcttttgtat gggatattgc 180
```

aaaaataaaa aggaaagaac cctcttnaan aaaaaa

216

&lt;210&gt; 220

&lt;211&gt; 380

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 220

```
cttacaaatt gcccccatgt gtaggggaca cagaaccctt tgagaaaact tagatttttg 60
tctgtacaaa gtctttgcct ttttccttct tcattttttt ccagtacatt aaatttgtca 120
atttcatctt tgagggaagac tgattagatg ggttgtgttt gtgttctgat ggagaaaaca 180
gcacccaag gactcagaag atgattttta cagttcagaa cagatgtgtg caatatttgt 240
gcatgtaata atgttgagtg gcagtcaaaa gtcattgatt ttattcttagt tcttcattac 300
tgcatgaaa aggaaaacct gtctgagaaa atgcctgaca gtttaattta aaactatggg 360
gtaagtcttt gacaaaaaaa                                     380
```

&lt;210&gt; 221

&lt;211&gt; 398

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 221

```
ggttagtaag ctgtcgactt tgtaaaaaag ttaaaaatga aaaaaaaagg aaaaatgaat 60
tgtatattta atgaatgaac atgtacaatt tgccactggg aggagggtcc tttttgttg 120
gtgagtcctg aagtgaattt cactgatgtt gatattcatt gtgtgtagtt ttatttcggt 180
cccagccccg tttcctttta ttttgaggct aatgccagct gcgtgtctag ttttgagtg 240
agtaaaatag aatcagcaaa tcaactcttat ttttcctcct tttccggtat tttttgggt 300
gtttctgtgg gagcagtgtg caccaactct tcctgtatat tgcctttttg ctggaaaatg 360
ttgtatgttg aataaaattt tctataaaaa ttaaaaaa                                     398
```

&lt;210&gt; 222

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (49)

&lt;223&gt; n=A,T,C or G

&lt;221&gt; unsure

&lt;222&gt; (64)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 222

```
ttcgataatt gatctcatgg gctttccctg gaggaaggt tttttttgnt gtttattttt 60
taanaacttg aaacttgtaa actgagatgt ctgtagcttt tttgcccac tgtagtgtat 120
gtgaagattt caaaacctga gagcactttt tctttgttta gaattatgag aaaggcacta 180
gatgacttta ggatttgcat ttttcccttt attgcctcat ttcttgtagc gccttggttg 240
ggagggaat ctgtttattt tttcctacaa ataaaaagct aagattctat atcgcaaaaa 300
a                                                                 301
```

&lt;210&gt; 223

&lt;211&gt; 200

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 223

gtaagtgcctt aggaagaaac tttgcaaaca tttaatgagg atacactgtt cattttttaa 60  
 attccttcac actgtaattt aatgtgtttt atattctttt gtagtaaaac aacataactc 120  
 agattttctac aggagacagt ggttttattt ggattgtcctt ctgtaatagg tttcaataaa 180  
 gctggatgaa cttaaaaaaa 200

&lt;210&gt; 224

&lt;211&gt; 385

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 224

gaaaggtttg atccggactc aaagaaagca aaggagtgtg agccgccatc tgctggagca 60  
 gctgtaactg caagacctgg acaagagatt cgtcagcgaa ctgcagctca aagaaacctt 120  
 tctccaacac cagcaagccc taaccagggc cctcctccac aagttccagt atctcctgga 180  
 ccaccaaagg acagttctgc ccctgggtgga ccccagaaa ggactgttac tccagcccta 240  
 tcatcaaatg tgttaccaag acatcttgga tcccctgcta cttcagtgcc tggaatgggt 300  
 aaacagagca cttaatgtta tttacagttt atattgtttt ctctgggttac caataaaacg 360  
 ggccattttc aggtggtaaa aaaaa 385

&lt;210&gt; 225

&lt;211&gt; 560

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 225

Met	Glu	Cys	Leu	Tyr	Tyr	Phe	Leu	Gly	Phe	Leu	Leu	Leu	Ala	Ala	Arg
1				5					10					15	
Leu	Pro	Leu	Asp	Ala	Ala	Lys	Arg	Phe	His	Asp	Val	Leu	Gly	Asn	Glu
			20					25					30		
Arg	Pro	Ser	Ala	Tyr	Met	Arg	Glu	His	Asn	Gln	Leu	Asn	Gly	Trp	Ser
		35				40					45				
Ser	Asp	Glu	Asn	Asp	Trp	Asn	Glu	Lys	Leu	Tyr	Pro	Val	Trp	Lys	Arg
	50				55					60					
Gly	Asp	Met	Arg	Trp	Lys	Asn	Ser	Trp	Lys	Gly	Gly	Arg	Val	Gln	Ala
65				70				75						80	
Val	Leu	Thr	Ser	Asp	Ser	Pro	Ala	Leu	Val	Gly	Ser	Asn	Ile	Thr	Phe
			85					90						95	
Ala	Val	Asn	Leu	Ile	Phe	Pro	Arg	Cys	Gln	Lys	Glu	Asp	Ala	Asn	Gly
		100						105					110		
Asn	Ile	Val	Tyr	Glu	Lys	Asn	Cys	Arg	Asn	Glu	Ala	Gly	Leu	Ser	Ala
	115					120						125			
Asp	Pro	Tyr	Val	Tyr	Asn	Trp	Thr	Ala	Trp	Ser	Glu	Asp	Ser	Asp	Gly
	130				135						140				
Glu	Asn	Gly	Thr	Gly	Gln	Ser	His	His	Asn	Val	Phe	Pro	Asp	Gly	Lys
145				150					155					160	
Pro	Phe	Pro	His	His	Pro	Gly	Trp	Arg	Arg	Trp	Asn	Phe	Ile	Tyr	Val
			165					170						175	
Phe	His	Thr	Leu	Gly	Gln	Tyr	Phe	Gln	Lys	Leu	Gly	Arg	Cys	Ser	Val
		180					185						190		
Arg	Val	Ser	Val	Asn	Thr	Ala	Asn	Val	Thr	Leu	Gly	Pro	Gln	Leu	Met
	195				200						205				
Glu	Val	Thr	Val	Tyr	Arg	Arg	His	Gly	Arg	Ala	Tyr	Val	Pro	Ile	Ala

210		215		220
Gln Val Lys Asp Val Tyr Val Val Thr Asp Gln Ile Pro Val Phe Val				
225		230		235
Thr Met Phe Gln Lys Asn Asp Arg Asn Ser Ser Asp Glu Thr Phe Leu				240
	245		250	255
Lys Asp Leu Pro Ile Met Phe Asp Val Leu Ile His Asp Pro Ser His				
	260		265	270
Phe Leu Asn Tyr Ser Thr Ile Asn Tyr Lys Trp Ser Phe Gly Asp Asn				
	275		280	285
Thr Gly Leu Phe Val Ser Thr Asn His Thr Val Asn His Thr Tyr Val				
	290		295	300
Leu Asn Gly Thr Phe Ser Leu Asn Leu Thr Val Lys Ala Ala Ala Pro				
305		310		315
Gly Pro Cys Pro Pro Pro Pro Pro Pro Pro Arg Pro Ser Lys Pro Thr				
	325		330	335
Pro Ser Leu Gly Pro Ala Gly Asp Asn Pro Leu Glu Leu Ser Arg Ile				
	340		345	350
Pro Asp Glu Asn Cys Gln Ile Asn Arg Tyr Gly His Phe Gln Ala Thr				
	355		360	365
Ile Thr Ile Val Glu Gly Ile Leu Glu Val Asn Ile Ile Gln Met Thr				
	370		375	380
Asp Val Leu Met Pro Val Pro Trp Pro Glu Ser Ser Leu Ile Asp Phe				
385		390		395
Val Val Thr Cys Gln Gly Ser Ile Pro Thr Glu Val Cys Thr Ile Ile				
	405		410	415
Ser Asp Pro Thr Cys Glu Ile Thr Gln Asn Thr Val Cys Ser Pro Val				
	420		425	430
Asp Val Asp Glu Met Cys Leu Leu Thr Val Arg Arg Thr Phe Asn Gly				
	435		440	445
Ser Gly Thr Tyr Cys Val Asn Leu Thr Leu Gly Asp Asp Thr Ser Leu				
	450		455	460
Ala Leu Thr Ser Thr Leu Ile Ser Val Pro Asp Arg Asp Pro Ala Ser				
465		470		475
Pro Leu Arg Met Ala Asn Ser Ala Leu Ile Ser Val Gly Cys Leu Ala				
	485		490	495
Ile Phe Val Thr Val Ile Ser Leu Leu Val Tyr Lys Lys His Lys Glu				
	500		505	510
Tyr Asn Pro Ile Glu Asn Ser Pro Gly Asn Val Val Arg Ser Lys Gly				
	515		520	525
Leu Ser Val Phe Leu Asn Arg Ala Lys Ala Val Phe Phe Pro Gly Asn				
	530		535	540
Gln Glu Lys Asp Pro Leu Leu Lys Asn Gln Glu Phe Lys Gly Val Ser				
545		550		555
				560

&lt;210&gt; 226

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 226

Ile Leu Ile Pro Ala Thr Trp Lys Ala

1

5

&lt;210&gt; 227

&lt;211&gt; 9



&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 227

Phe Leu Leu Asn Asp Asn Leu Thr Ala

1

5

&lt;210&gt; 228

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 228

Leu Leu Gly Asn Cys Leu Pro Thr Val

1

5

&lt;210&gt; 229

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 229

Lys Leu Leu Gly Asn Cys Leu Pro Thr Val

1

5

10

&lt;210&gt; 230

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 230

Arg Leu Thr Gly Gly Leu Lys Phe Phe Val

1

5

10

&lt;210&gt; 231

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 231

Ser Leu Gln Ala Leu Lys Val Thr Val

1

5

&lt;210&gt; 232

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 232

Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr Ser Arg Tyr Phe

5

10

15

Phe Ser Phe Ala

20

<210> 233  
<211> 21  
<212> PRT  
<213> Homo sapiens

<400> 233  
Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys Val His Val  
5 10 15

Asn His Ser Pro Ser  
20

<210> 234  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 234  
Phe Leu Val Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe  
5 10 15

Asp Pro Asp Gly  
20

<210> 235  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 235  
Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu Phe Ile Pro  
5 10 15

Pro Asn Ser Asp  
20

<210> 236  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 236  
Ile Gln Asp Asp Phe Asn Asn Ala Ile Leu Val Asn Thr Ser Lys Arg  
5 10 15

Asn Pro Gln Gln  
20

<210> 237

<211> 21  
<212> PRT  
<213> Homo sapiens

<400> 237  
Arg Asn Ser Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu  
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Phe Ile Pro Pro Asn  
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<210> 238  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 238  
Thr His Glu Ser His Arg Ile Tyr Val Ala Ile Arg Ala Met Asp Arg  
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Asn Ser Leu Gln  
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<210> 239  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 239  
Arg Asn Pro Gln Gln Ala Gly Ile Arg Glu Ile Phe Thr Phe Ser Pro  
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Gln Ile Ser Thr  
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<210> 240  
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<212> PRT  
<213> Homo sapiens

<400> 240  
Gly Gln Ala Thr Ser Tyr Glu Ile Arg Met Ser Lys Ser Leu Gln Asn  
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Ile Gln Asp Asp Phe  
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<210> 241  
<211> 20  
<212> PRT  
<213> Homo sapiens

&lt;400&gt; 241

Glu Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser  
5 10 15

Val Leu Gly Val  
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&lt;210&gt; 242

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 242

Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn Ile  
5 10 15

Gln Met Asn Ala  
20

&lt;210&gt; 243

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 243

Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile Pro Gly  
5 10 15

Ser His Ala Met  
20

&lt;210&gt; 244

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 244

Ala Val Pro Pro Ala Thr Val Glu Ala Phe Val Glu Arg Asp Ser Leu  
5 10 15

His Phe Pro His  
20

&lt;210&gt; 245

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 245

Lys Pro Gly His Trp Thr Tyr Thr Leu Asn Asn Thr His His Ser Leu

117

5 10 15

Gln Ala Leu Lys  
20

<210> 246  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 246  
Asn Leu Thr Phe Arg Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys  
5 10 15

Pro Gly His Trp  
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<210> 247  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 247  
Leu His Phe Pro His Pro Val Met Ile Tyr Ala Asn Val Lys Gln Gly  
5 10 15

Phe Tyr Pro Ile  
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<210> 248  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 248  
Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu Leu Asp Asp Gly Ala  
5 10 15

Gly Ala Asp Val  
20

<210> 249  
<211> 20  
<212> PRT  
<213> Homo sapiens

<400> 249  
Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val Thr Ala Thr Val Glu Pro  
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Glu Thr Gly Asp

20

<210> 250  
 <211> 20  
 <212> PRT  
 <213> Homo sapiens

<400> 250  
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Leu Thr Phe Arg  
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<210> 251  
 <211> 20  
 <212> PRT  
 <213> Homo sapiens

<400> 251  
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Val Pro Pro Ala  
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<210> 252  
 <211> 153  
 <212> PRT  
 <213> Homo sapien

<400> 252  
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                           20                          25                          30  
 Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly  
                           35                          40                          45  
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys  
   50                          55                          60  
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp  
  65                          70                          75                          80  
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr  
                           85                          90                          95  
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala  
                           100                          105                          110  
 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu  
                           115                          120                          125  
 Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser  
                           130                          135                          140  
 Glu Asn Gln Gly Ala Phe Lys Gly Met  
 145                          150

<210> 253  
 <211> 462  
 <212> DNA  
 <213> Homo sapien

<400> 253  
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<210> 254  
 <211> 8031  
 <212> DNA  
 <213> Homo sapien

<400> 254  
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&lt;210&gt; 255

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(401)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 255

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&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

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&lt;222&gt; (1)...(401)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 256

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&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(401)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 257

atgtatgtaa	aacacttcat	aaaatgtaaa	gggctataac	aaatatgtta	taaagtgatt	60
ctctcagccc	tgaggtatac	agaatcattt	gcctcagact	gctgttggat	tttaaaattt	120
ttaaaatata	tgctaagtaa	tttgctatgt	cttctcccac	actatcaata	tgctgtcttc	180
taacaggctc	cccactttct	tttaatgtgc	tgttatgagc	tttggacatg	agataaccgt	240
gcctgttcag	agtgtctaca	gtaagagctg	gacaaaactct	ggagggacac	agtctttgag	300
acagctcttt	tggttgcttt	ccacttttct	gaaaggttca	cagtaacctt	ctagataata	360
gaaactccca	gttaaagcct	angctancaa	ttttttttag	t		401

&lt;210&gt; 258

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

```

<400> 258
ggagcgctag gtcggtgtac gaccgagatt aggggtgcgtg ccagctccgg gaggccgcgg      60
tgagggggccg ggcccaagct gccgacccga gccgatcgtc agggtcgccca gcgcctcagc      120
tctgtggagg agcagcagta gtcggagggt gcaggatatt agaaatggct actccccagt      180
caattttcat ctttgcaatc tgcattttta tgataacaga attaattctg gcctcaaaaa      240
gctactatga tatcttaggt gtgccaaaat cggcatcaga gcgccaaatc aagaaggcct      300
ttcacaagtt ggccatgaag taccaccctg acaaaaataa gacccagatg ctgaagcaaa      360
attcagagag attgcagaag catatgaaac actctcagat g                               401

```

```

<210> 259
<211> 401
<212> DNA
<213> Homo sapien

```

```

<400> 259
attgggtttg gaggaggat gatgacagag gaatgccctt tggccatcac ggttttgatt      60
ctccagaata ttgtgggttt gatcatcaat gcagtcatgt taggtgcat ttcatgaaa      120
acagctcagg ctacagaag ggcagaaact ttgattttca gccgccatgc tgtgattgcc      180
gtccgaaatg gcaagctgtg cttcatgttc cgagtgggtg acctgaggaa aagcatgac      240
attagtgcct ctgtgcgcat ccagggtggtc aagaaaacaa ctacacctga aggggagggtg      300
gttcctattc accaactgga cattcctgtt gataacccaa tcgagagcaa taacattttt      360
ctgggtggccc ctttgatcat ctgccacgtg attgacaagc g                               401

```

```

<210> 260
<211> 363
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(363)
<223> n = A,T,C or G

```

```

<400> 260
aggaganang gagggggana tgaatagggga tggagaggga natagtggat gagcagggca      60
canggagagg aancagaaag gagaggcaag acaggggagac acacancaca nangangana      120
caggtggggg ctgggggtggg gcatggagag ccttttnangt cncccaggcc accctgctct      180
cgctggncctg ttgaaaccca ctccatggct tectgccact gcagttgggc ccagggctgg      240
cttatnctg gaatgcaagt ggctgtggct tggagcctcc cctctggnnn anggaaannn      300
attgctccct tatctgcttg gaatatctga gtttttccan cccggaaata aaacacacac      360
aca                               363

```

```

<210> 261
<211> 401
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

```

```

<400> 261
cggctctccg ccgctctccc ggggtttcgg ggcacttggg tcccacagtc tggctctgct      60
tcaccttccc ctgacctgag tagtcgcat ggcacagggt ctgagaggca ctgngactga      120

```

```

cttccctgga tttgatgagc gggctgatgc anaaactctt cggaaggcta tgaaaggctt 180
gggcacagat gaggagagca tcctgactct gttgacatcc cgaagtaatg ctcagcgcca 240
ggaaatctct gcagctttta agactctggt tggcagggat cttctggatg acctgaaatc 300
agaactaact ggaaaatttg aaaaattaat tgtggctctg atgaaaccct ctcggtttta 360
tgatgcttat gaactgaaac atgccttgaa gggagctgga a 401

```

<210> 262

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 262

```

agtctanaac atttctaata ttttgngctt tcatatatca aaggagatta tgtgaaacta 60
tttttaaata ctgtaaagtg acatatagtt ataagatata tttctgtaca gtagagaaag 120
agtttataac atgaagaata ttgtaccatt atacattttc attctcgatc tcataagaaa 180
ttcaaaagaa taatgataga ggtgaaaata tgtttacttt ctctaaatca agcctagtgt 240
tcaactcaaa aattatgntg catagtttta ttttgaattt aggttttggg actacttttt 300
tccancttca atgagaaaat aaaatctaca actcaggagt tactacagaa gttctaanta 360
tttttttgc tannagcnaa aaatataaac atatgaaaat g 401

```

<210> 263

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 263

```

ctgtccgacc aagagaggcc ggccgagccc gaggcttggg cttttgcttt ctggcggagg 60
gatctgcggc ggtttaggag gcggcgctga tcctgggagg aagaggcagc tacggcggcg 120
gcggcggttg cggctagggc ggccggaat aaaggggccc ccgcccgggtg atgcggtgac 180
cactgcggca ggcccaggag ctgagtgggc cccggccctc agcccgtccc gncggaccgc 240
ctttcctcaa ctctccatct tctcctgccg accgagatcg ccgaggcggn ctcaggctcc 300
ctanccctt ccccgccct tcccncccc cgtccccgcc ccggggggcg ccgccaccgc 360
cctcccacca tggtcttgaa ganaatccac aaggaattga a 401

```

<210> 264

<211> 401

<212> DNA

<213> Homo sapien

<400> 264

```

aacaccagcc actccaggac cctgaaggc ctctaccagg tcaccagtgt tctgcgccta 60
aagccacccc ctggcagaaa cttcagctgt gtgttctgga atactcacgt gagggaaactt 120
actttggcca gcattgacct tcaaagtcag atggaaccca ggaccatcc aacttggctg 180
cttcacattt tcatccctc ctgcatcatt gctttcattt tcatagccac agtgateagcc 240
ctaagaaac aactctgtca aaagctgtat tcttcaaaag acacaacaaa aagacctgtc 300

```

accacaacaa agaggggaagt gaacagtgct gtgaatctga acctgtgggc ttgggagcca 360  
gggtgacctg atatgacatc taaagaagct tctggactct g 401

<210> 265  
<211> 271  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(271)  
<223> n = A,T,C or G

<400> 265  
gccacttcct gtggacatgg gcagagcgct gctgccagtt cctggtagcc ttgaccacna 60  
cgctgggggg tctttgtgat ggtcatgggt ctcatctgca cttgggggtg tgggattcaa 120  
gttagaagtt tctagatctg gccgggcgca gtggctcaca cctgtaatcc cagcacttta 180  
ggaggctgag gcaggcgat catgaggcca ggagatcgag accgtcctgg ctaacacagt 240  
gaaacccctg ctctactaaa aatacaaaaa a 271

<210> 266  
<211> 401  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(401)  
<223> n = A,T,C or G

<400> 266  
attcataaat ttagctgaaa gatactgatt caatttgtat acagngaata taaatgagac 60  
gacagcaaaa ttttcatgaa atgtaaaata tttttatagt ttgttcatac tatatgaggt 120  
tctattttta atgactttct ggatttttaa aaatttcttt aaatacaatc atttttgtaa 180  
tattttatct atgcttatga tctagataat tgcagaatat cattttatct gactctgtct 240  
tcataagaga gctgtggcgg aattttgaac atctgttata gggagtgtac aaattagaag 300  
gcaatgtgga aaaacaattc tgggaaagat ttctttatat gaagtccttg ccactagcca 360  
gccatcctaa ttgatgaaag ttatctgttc acaggcctgc a 401

<210> 267  
<211> 401  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(401)  
<223> n = A,T,C or G

<400> 267  
gaagaggcat cacctgatcc cggagacctt tggagttaag aggcggcgga agcgagggcc 60  
tgtggagtcg gatcctcttc ggggtgagcc agggctcgcg cgcgcggtg tctcanaact 120  
catgcagctg ttcccgcgag gctgtttga ggacgcgctg cgcgccatcg tgctgaggag 180  
ccaggtgtac agccttgtgc ctgacaggac cgtggccgac cggcagctga aggagcttca 240  
agagcanggg gagacaaaat cgtccagctg ggcttcnact tggatgccca tggaanttat 300

tctttcnctt ganggactta cnngggaccc aagaanccct tncaaggggc ccttngtgga 360  
tgggncccgga aaccccnnta tttgcccttg ggggggncca a 401

<210> 268  
<211> 223  
<212> DNA  
<213> Homo sapien

<400> 268  
tcgccatggt ggccaggctg gtcttgaact cctgacttta agtgatccac cgcctcaac 60  
ctcccaaagt gctgggatta cagggtgtgag ccaccgcgc tggcctgata catactttta 120  
gaatcaagta gtcacgcact tttctgttc atttttctaa aaagtaaata tacaagtgtt 180  
ttgttttttg tttttttgt ttgtttgtt ctgtttttt ttt 223

<210> 269  
<211> 401  
<212> DNA  
<213> Homo sapien

<400> 269  
actatgtaaa ccacattgta ctttttttta ctttggcaac aaatatattat acatacaaga 60  
tgctagtcca tttgaatatt tctccaact tatccaagga tctccagctc taacaaaatg 120  
gtttattttt atttaaatgt caatagttgt tttttaaaat ccaaatcaga ggtgcaggcc 180  
accagttaaa tgccgtctat caggttttgt gccttaagag actacagagt caaagctcat 240  
ttttaaaagga gtaggacaaa gttgtcacag gttttgttg ttgtttttat tgcccccaaa 300  
attacatggt aatttccatt tatatcaggg attctattta cttgaagact gtgaagttgc 360  
cattttgtct cattgttttc tttgacataa ctaggatcca t 401

<210> 270  
<211> 401  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(401)  
<223> n = A,T,C or G

<400> 270  
tggctgttga ttcacctcag cactgcttgg tatctgcacc ctacctctct ttagaggctg 60  
ccttgtcaac tgaaaaatgc acctgacttc gagcaagact ctttccttag gttctggatc 120  
tgtttgagcc ccattggcact gagctggaat ctgagggctc tgttccaagg atgtgatgat 180  
gtgggagaat gttctttgaa agagcagaaa tccagtctgc atggaaacag cctgtagagn 240  
agaagtttcc agtgataagt gttcactgtt ctaaggaggt acaccacagc tacctgaatt 300  
ttcccaaaat gagtgcttct gtgcgttaca actggccttt gtacttgact gtgatgactt 360  
tgttttttct tttcaattct anatgaacat gggaaaaaat g 401

<210> 271  
<211> 329  
<212> DNA  
<213> Homo sapien

<400> 271  
ccacagcctc caagtcaggt ggggtggagt ccagagctg cacagggttt ggcccaagtt 60  
tctaaggagag gcacttcctc ccctcgccca tcagtgccag ccctgctgg ctggtgctg 120

```

agccccctcag acagccccct gccccgcagg cctgccttct cagggacttc tgcggggcct      180
gaggcaagcc atggagttag acccaggagc cggacacttc tcaggaaatg gcttttccca      240
acccccagcc cccacccggg ggttcttcct gttctgtgac tgtgtatagt gccaccacag      300
cttatggcat ctcattgagg acaaaaaaa      329

```

<210> 272

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 272

```

nggctgntaa cntcggaggt nacttcctgg actatcctgg agacccccctc cgcttccacg      60
nncatnatat cntcatngc tgggcccntn angacacnat cccactccaa cacctgngng      120
atgctggncn cctnggaacc ancntcagaa ngaccctgnt cntntgtntt ccgcaanctg      180
aagnnaangc gggntacacc tncntgcant ggnccacnct gcnggggaact ntacacacct      240
acgggatgtg gctgcgcan gagccaagag cntttctgga tgattcccca gcctcttgnn      300
agggantcta caacattgct nnntaccttt ntccnncngc nnntnntgga ntacaggngn      360
tnntaacact acatcttttt tactgcncn tncctgggtg g      401

```

<210> 273

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 273

```

cagcaccatg aagatcaaga tcatcgacc cccagagcgc aagtactcgg tgtggatcgg      60
tggctccatc ctggcctcac tgtccacctt ccagcagatg tggattagca agcaggagta      120
cgacgagtcg ggccctccca tegtccaccg caaatgcttc taaacggact cagcagatgc      180
gtagcatttg ctgcatgggt taattgagaa tagaaatttg cccctggcaa atgcacacac      240
ctcatgctag cctcacgaaa ctggaataag ccttcgaaaa gaaattgtcc ttgaagcttg      300
tatctgatat cagcactgga ttgtagaact tgttgctgat tttgacctg tattgaagtt      360
aactgttccc cttggtatta acgtgtcagg gctgagtnt c      401

```

<210> 274

<211> 401

<212> DNA

<213> Homo sapien

<400> 274

```

ccaccacac ccaccgcgc ctcgttcgcc tcttctcgg gagccagtcc gcgccaccgc      60
cgccgcccag gccatcgcca cctccgcag ccatgtccac caggctcgtg tcctcgtcct      120
cctaccgcag gatgttcggc ggcccgggca ccgcgagccg gccgagctcc agccggagct      180
acgtgactac gtccaccgc acctacagcc tgggcagcgc gctgcgcccc agcaccagcc      240
gcagccteta cgctcgtcc ccgggcggcg tgtatgccac gcgtcctct gccgtgcgcc      300
tgccgagcag cgtgcccggg gtgcggctcc tgcaggactc ggtggacttc tcgctggccg      360

```

acgccatcaa caccgagttc aagaacaccc gcaccaacga g 401

<210> 275  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 275  
 ccacttccac cactttgtgg agcagtgcct tcagcgcaac ccggatgccca ggtatccctg 60  
 ctggcctggg cctgggcttc gggagagcag aggggtgctca ggagggtaag gccaggggtg 120  
 gaagggactt acctcccaa ggttctgcag gggaaatctgg agctacacac aggagggatc 180  
 agctcctggg tgtgtcagag gccagcctgg ggagctctgg ccactgcttc ccatgagctg 240  
 agggagaggg agaggggacc cgaggctgag gcataagtgg caggatttcg ggaagctggg 300  
 gacacggcag tgatgctgcg gtctctctc ccctttccct ccaggcccag tgccagcacc 360  
 ctctgaacc actctttctt caagcagatc aagcgacgtg c 401

<210> 276  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(401)  
 <223> n = A,T,C or G

<400> 276  
 tctgatattg ntacccttga gccacctaag ttagaagaaa ttggaaatca agaagttgtc 60  
 attgttgaag aagcacagag ttcagaagac tttaacatgg gctcttctc tagcagccag 120  
 tatactttct gtcagccaga aactgtattt tcatctcagc ctagtatga tgaatcaagt 180  
 agtgatgaaa ccagtaatca gccagtcct gcctttagac gacgccgtgc taggaagaag 240  
 accgtttctg cttcagaatc tgaagaccgg ctagtgtgtg aacaagaaac tgaaccttct 300  
 aaggagttga gtaaactgca gttcagtagt ggtctcaata agtgtgttat acttgctttg 360  
 gtgattgcaa tcagcatggg atttggccat ttctatggga c 401

<210> 277  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(401)  
 <223> n = A,T,C or G

<400> 277  
 aactttggca acatatctca gcaaaaacta cagctatggt attcatgccca aaataaaagc 60  
 tgtgcagagg agtggctgca atgaggtcac aacgggtggg gatgtaaaag agatcttcaa 120  
 gtcctcatca cccatccctc gaactcaagt cccgctcatt acaaattctt cttgccagt 180  
 tccacacatc ctgccccatc aagatgttct catcatgtgt tacgagnggc gctcaaggat 240  
 gatgcttctt gaaaattgct tagttgaaaa atggagagat cagcttagta aaagatccat 300  
 acagtgggaa gagaggctgc aggaacagcg ganaacagtt caggacaaga agaaaacagc 360  
 cgggcgcacc agtcgtagta atccccccaa accaaaggga a 401

<210> 278



<211> 401  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(401)  
<223> n = A,T,C or G

<400> 278  
aatgagtgtg agaccacaaa tgaatgccgg gaggatgaaa tgtgttgga ttatcatggc 60  
ggcttcggtt gttatccacg aaatccttgt caagatccct acattctaac accagagaac 120  
cgatgtgttt gccagtcctc aaatgccatg tgccgagaac tgccccagtc aatagtctac 180  
aaatacatga gcatccgacg tgataggtct gtgccatcag acatcttcca gatacaggcc 240  
acaactatth atgccaacac catcaatact tttcggatta aatctggaaa tgaaaatgga 300  
gagtctacct acgacaacaa anccctgtaa gtgcaatgct tgtgtctcgtg aagncattat 360  
caggaccaag agaacatatac gtggacctgg agatgctgac a 401

<210> 279  
<211> 401  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(401)  
<223> n = A,T,C or G

<400> 279  
aaattattgc ctctgataca tacctaagtn aacanaacat taatacctaa gtaaacataa 60  
cattacttgg aggggttcag nttctaantg aaactgtatt tgaaactttt aagtatactt 120  
taggaaacaa gcatgaacgg cagtctagaa taccagaaac atctacttgg gtagcttggn 180  
gccattatcc tgtggaatct gatatgtctg gnagcatgtc attgatggga catgaagaca 240  
tctttggaaa tgatgagatt atttcctgtg ttaaaaaaaaa aaaaaatctt aaattcctac 300  
aatgtgaaac tgaaactaat aattttgatc ctgatgtatg ggacagcgta tctgtaccag 360  
gctctaaata acaaaaagnta gggngacaag nacatgttcc t 401

<210> 280  
<211> 326  
<212> DNA  
<213> Homo sapien

<400> 280  
gaagtggaat tgtataattc aattcgataa ttgatctcat gggctttccc tggaggaaag 60  
gttttttttg ttgttttttt ttttaagaact tgaaacttgt aaactgagat gtctgtagct 120  
tttttgccca tctgtagtgt atgtgaagat ttcaaaacct gagagcactt tttctttgtt 180  
tagaattatg agaaaggcac tagatgactt taggatttgc atttttccct ttattgcctc 240  
atttcttgtg acgccttgtt ggggagggaa atctgtttat tttttcctac aaataaaaag 300  
ctaagattct atatcgcaaa aaaaaa 326

<210> 281  
<211> 374  
<212> DNA  
<213> Homo sapien

```

<400> 281
caacgcggtt gcaaatatc ccttggtagc ctacttcctt acccccgaat attggtaaga      60
tcgagcaatg gcttcaggac atgggttctc ttctcctgtg atcattcaag tgctcactgc      120
atgaagactg gcttgctctc gtgtttcaac ctcaccaggg ctgtctcttg gtccacacct      180
cgctccctgt tagtgccgta tgacagcccc catcaaata ccttggccaa gtcacgggtt      240
ctctgtggtc aaggttgggt ggctgattgg tggaaagtag ggtggaccaa aggaggccac      300
gtgagcagtc agcaccagtt ctgcaccagc agcgctccg tcctagtggg tgttcctggt      360
tctcctggcc ctgg                                     374

```

```

<210> 282
<211> 404
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(404)
<223> n = A,T,C or G

```

```

<400> 282
agtgtggtgg aattcccgc tcctanncgc cgactcacac aaggcagagt ngccatggag      60
aaaattccag tgtcagcatt cttgctcctt gtggccctct cctacactct ggccagagat      120
accacagtca aacctgnagc caaaaaggac acaaaggact ctcgacccaa actgccccan      180
accctctcca gaggttgggg tgaccaactc atctggactc anacatatga agaagctcta      240
tataaatcca agacaagcaa caaaccttg atgattattc atcacttgga tgagtgccca      300
cacagtcaag ctttaaagaa agtgtttgct gaaaataaag aaatccagaa attggcagag      360
cagtttgtcc tcctcaatct ggtttatgaa acaactgaca aaca                                     404

```

```

<210> 283
<211> 184
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(184)
<223> n = A,T,C or G

```

```

<400> 283
agtgtggtgg aattcacttg cttaanttgt gggcaaaaga gaaaaagaag gattgatcag      60
agcattgtgc aatacagttt cattaactcc ttccctcgtc cccccaaaaa tttgaatttt      120
tttttcaaca ctcttacacc tgttatggaa aatgtcaacc tttgtaagaa aaccaaataa      180
aaaa                                     184

```

```

<210> 284
<211> 421
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(421)
<223> n = A,T,C or G

```

```

<400> 284

```

ctattaatcc tgccacaata tttttaatta cgtacaaaga tctgacatgt caccagggga 60  
cccatttcac ccactgctct gtttggccgc cagtcttttg tctctctctt cagcaatggg 120  
gaggcgata ccctttcctc ggggaanana aatccatggg ttgttgccct tgccaataac 180  
aaaaatgttg gaaagtcgag tggcaaagct gttgccattg gcattcttca cgtgaaccac 240  
gtcaaaagat ccagggtgcc tctctctgtt ggtgatcaca ccaattcttc ctagggttagc 300  
acctccagtc accatacaca ggttaccagt gtcgaacttg atgaaatcag taatcttgcc 360  
agtctctaaa tcaatctgaa tggatcatt caccttgatg aggggatcgg ggtagcggat 420  
g 421

<210> 285

<211> 361

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (361)

<223> n = A,T,C or G

<400> 285

ctgggtggta actctttatt tcattgtccg gaanaaagat gggagtggga acagggtgga 60  
cactgtgcag gcttcagctt ccactccggg caggattcag gctatctggg accgcagggg 120  
ctgccagggtg cacagccctg gctcccgagg caggcaggca aggtgacggg actggaagcc 180  
cttttcanag ccttggagga gctgggtccgt ccacaagcaa tgagtgccac tctgcagttt 240  
gcaggggatg gataaacagg gaaacactgt gcattcctca cagccaacag tgtaggtctt 300  
ggtgaagccc cggcgctgag ctaagctcag gctgttccag ggagccacga aactgcaggt 360  
a 361

<210> 286

<211> 336

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (336)

<223> n = A,T,C or G

<400> 286

tttgagtggc agcgccttta tttgtggggg ccttcaaggg agggtcgtgg ggggcagcgg 60  
ggaggaanag ccganaaact gtgtgaccgg ggcctcaggt ggtgggcatt gggggctcct 120  
cttgcanatg cccattggca tcaccggtgc agccattggt ggcagcgggt accggtcctt 180  
tcttgttcaa catagggtag gtggcagcca cgggtccaac tcgcttgagg ctggggcctg 240  
ggcgtccat tttgtgttcc angagcatgt ggttctgtgg cgggagcccc acgcagggcc 300  
tgaggatggt ctcgatgcag ctgcgctggc ggaaaa 336

<210> 287

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (301)

<223> n = A,T,C or G

&lt;400&gt; 287

tggttaccaa	atttntttat	ttgaaggaat	ggnacaaatc	aaanaactta	agnggatgtt	60
ttggtacaac	ttatanaaaa	ggnaaaggaa	accccaacat	gcatgcncgt	ccttgngac	120
cagggagtc	acccacggc	tatggggaaa	ttancccgag	gcttancttt	cattatcact	180
gtctcccagg	gngngcttgt	caaaaanata	ttcncccaag	ccaaattcgg	gcgctcccat	240
nttgcncaa	g	ggtcacccaa	ttctttgatg	gctttcacct	gctcattcag	300
						301

&lt;210&gt; 288

&lt;211&gt; 358

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(358)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 288

aagtttttaa	acttttttatt	tgcatattaa	aaaaattgng	cattccaata	attaaaatca	60
tttgaacaaa	aaaaaaaaatg	gcactctgat	taaactgcat	tacagcctgc	aggacacctt	120
gggccagctt	ggttttactc	tanatttcac	tgctgtccca	ccccacttct	tccacccac	180
ttcttcttc	accaacatgc	aagttctttc	cttcctgcc	agccanatag	atagacagat	240
gggaaaggca	ggcgccgcct	tcgttgtcag	tagttctttg	atgtgaaagg	ggcagcacag	300
tcattttaa	ac	ctctttgcat	cttacaaagt	taaacagcta	aaagaagt	358

&lt;210&gt; 289

&lt;211&gt; 462

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(462)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 289

ggcatcagaa	atgctgttta	tttctctgct	gctcccaagc	tggttgccct	ttgcagagga	60
gcagacaaca	gatgcatagt	tgggganaaa	gggaggacag	gttccaggat	agaggggtgca	120
ggctgaggga	ggaagggtaa	naggaaggaa	ggccatcctg	gatccccaca	tttcagtctc	180
anatgaggac	aaagggactc	ccaagcccc	aatcatcan	aaaacaccaa	ggagcaggag	240
gagcttgagc	aggccccagg	gagcctcana	gccataccag	ccactgtcta	cttcccatcc	300
tcctctccca	ttcctgtct	gcttcanacc	acctcccagc	taagccccag	ctccattccc	360
ccaatcctgg	cccttgccag	cttgacagtc	acagtgcctg	gaattccacc	actgagggtt	420
ctcccagttg	gattaggacg	tcgccctgtt	agcatgctgc	cc		462

&lt;210&gt; 290

&lt;211&gt; 481

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(481)

<223> n = A,T,C or G

<400> 290

tactttccta aactttatta aagaaaaaag caataagcaa tggnggtaaa tctctanaac	60
ataccecaatt ttctgggctt cctccccga gaatgtgaca ttttgatttc caaacatgcc	120
anaagtgtat ggttcccaac tgtactaaag taggtganaa gctgaagtcc tcaagtgttc	180
atcttccaac ttttccagc ctgtggtctg tctttggatc agcaataatt gcctgaacag	240
ctactatggc ttctgtgatt tttgtctgta gctctctgag ctctctatg tgcagcaatc	300
gcanaatttg agcagcttca ttaanaactg catctcctgt gtcaaaacca anaatatgtt	360
tgtctaaagc aacaggttaag ccctcttttg tttgatttgc cttancaact gcatcctgtg	420
tcaggcgctc ctgaaccaa atccgaattg ccttaagcat taccaggtta tcatcatgac	480
g	481

<210> 291

<211> 381

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(381)

<223> n = A,T,C or G

<400> 291

tcataagtaat gtaaaacat ttgtttaatt ctaaatcaaa tcactttcac aacagtgaac	60
attagtgtact ggtaagng tgccactgta catatcatca tttctgact ggggtcagga	120
cctggtccta gtccacaagg gtggcaggag gaggtggag gctaanaaca cagaaaacac	180
acaaaanaaa ggaagctgc cttggcanaa ggatgagng gtgagcttgc cgaaggatgg	240
tggaagggg gctccctgtt ggggcccagc caggagtccc aagtcagctc tcctgcctta	300
cttagctcct ggcanaggtt gagtggggac ctacgaggtt caaaatcaaa tggcatttgg	360
ccagcctggc ttactaaca g	381

<210> 292

<211> 371

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(371)

<223> n = A,T,C or G

<400> 292

gaaaaaataa tccgtttaat tgaaaaacct gnaggatact attccactcc cccanatgag	60
gaggctgagg anaccaaacc cctacatcac ctctagacca cttctgatac tcttcacgag	120
gcagcaggca aagacaattc ccaaaacctc naaaaagca attccaaggg ctgctgcagc	180
taccaccanc acatttttcc tcagccagcc cccaatcttc tccacacagc cctccttatg	240
gatcgcttc tcgttgaaat taatcccaca gccacagta acattaatgc ancaggagtc	300
ggggactcgg ttcttgaca tggaaggat tttctcccaa tctgtgtagt tagcagcccc	360
acagcactta a	371

<210> 293

<211> 361

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(361)  
 <223> n = A,T,C or G

<400> 293  
 gattttaaag aaaacacttt attgttcagc aattaaaagt tagccaaata tgtatttttc 60  
 tccataattt attgngatgt tatcaacatc aagtaaaatg ctcatTTTTca tcatTTgctt 120  
 ctgttcatgt tttcttgaac acgtcttcaa ttttcttcc aaaatgctgc atgccacact 180  
 tgaggtaacg aagcanaagt atttttaaac atgacagcta anaacattca tctacagcaa 240  
 cctatatgct caatacatgc cgcgtgatcc tagtagtttt ttcacaacct tctacaagtt 300  
 tttggaaaac atctgttatg atgactttca tacaccttca cctcaaaggc tttcttgca 360  
 c 361

<210> 294  
 <211> 391  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(391)  
 <223> n = A,T,C or G

<400> 294  
 tatttttaaag ttttaattatg attcanaaaa aatcgagcga ataactttct ctgaaaaaat 60  
 atattgactc tgtatanacc acagttattg gggganaagg gctggtaggt taaattatcc 120  
 tattttttat tctgaaaatg atattaatan aaagtcctcg ttccagtctg attataaaga 180  
 tacatatgcc caaaatggct ganaataaat acaacaggaa atgcaaaagc tgtaaagcta 240  
 agggcatgca ananaaaatc tcanaatacc caaagnggca acaaggaacg tttggctgga 300  
 atttgaagtt atttcagtca tctttgtctt tggctccatg tttcaggatg cgtgtgaact 360  
 cgatgtaatt gaaattcccc tttttatcaa t 391

<210> 295  
 <211> 343  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(343)  
 <223> n = A,T,C or G

<400> 295  
 ttcttttgtt ttattgataa cagaaactgt gcataattac agatttgatg aggaatctgc 60  
 aaataataaa gaatgtgtct actgccagca aaatacaatt attccatgcc ctctcaacat 120  
 acaaatatag agttcttcac accanatggc tctggtgtaa caaagccatt ttanatgttt 180  
 aattgtgctt ctacaaaacc ttcanagcat gaggtagttt cttttaccta cnatattttc 240  
 cacatttcca ttattacact tttagtgagc taaaatcctt ttaacatagc ctgcggatga 300  
 tctttcacaa aagccaagcc tcatttacaagggtttatt tct 343

<210> 296  
 <211> 241  
 <212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(241)

<223> n = A,T,C or G

<400> 296

ttcttgata ttggtgttt ttgtgaaaaa gtttttgttt ttcttctcag tcaactgaat	60
tatttctcta ctttgccctc ctgatgcccc catgananaa cttaanataa tttctaacag	120
cttcactttt ggaaaaaaa aaaacctgtt ttctcatgg aaccccagga gttgaaagtg	180
gatanatcgc tctcaaaatc taaggctctg ttcagcttta cattatgtta cctgacgttt	240
t	241

<210> 297

<211> 391

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(391)

<223> n = A,T,C or G

<400> 297

gttgtggctg anaatgctgg agatgctcag ttctctccct cacaaggtag gccacaaatt	60
cttgggtgtg ccctcacatc tgggtctctc aggcaccagc catgcctgcc gaggagtgtc	120
gtcaggacan accatgtccg tgctaggccc aggcacagcc caaccactcc tcatccaagt	180
ctctcccagg tttctggtcc cgatgggcaa ggatgacccc tccagtggct ggtacccac	240
catcccacta cccctcacat gctctcactc tccatcaggt ccccaatcct ggcttccctc	300
ttcacgaact ctcaaagaaa aggaaggata aaacctaaat aaaccagaca gaagcagctc	360
tggaaaagta caaaaagaca gccagaggtg t	391

<210> 298

<211> 321

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(321)

<223> n = A,T,C or G

<400> 298

caagccaaac tgtntccagc tttattaaan atactttcca taaacaatca tggatattca	60
ggcaggacat gggcanacaa tcgttaacag tataacaaca ctttcaaact cccttnttca	120
atggactacc aaaaaatcaaa aagccactat aaaacccaat gaagtcttca tctgatgtc	180
tgaacagggg aagtttaaaag ngagggttga catttcacat ttagcatgtt gttaacaac	240
ttttacaag ccgaccttga ctttcaggaa gtgaaatgaa aatggcanaa tttatctgaa	300
natccacaat ctaaaaatgg a	321

<210> 299

<211> 401

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(401)  
 <223> n = A,T,C or G

<400> 299  
 tatcataaag agtgttgaag tttatattt atagcaccat tgagacattt tgaaattgga 60  
 attggtaaaa aaataaaaaca aaaagcattt gaattgtatt tggnggaaca gcaaaaaaag 120  
 agaagtatca tttttctttg tcaaattata ctgtttccaa acatttttga aataaataac 180  
 tggaaatttg tcggtcactt gcaactggtg acaagattag aacaagagga acacatatgg 240  
 agttaaattt tttttgttgg gatttcanat agagtttggg ttataaaaag caaacagggc 300  
 caacgtccac accaaaattct tgatcaggac caccaatgtc atagggngca atatctacaa 360  
 taggtagtct cacagccttg cgtgttcgat attcaaagac t 401

<210> 300  
 <211> 188  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(188)  
 <223> n = A,T,C or G

<400> 300  
 tgaatgcttt gtcataataa gaaagttaaa gtgcaataat gtttgaanac aataagtggg 60  
 ggtgtatctt gtttctaata agataaaact ttttgtcttt gctttatctt attagggagt 120  
 tgtatgtcag tgtataaaac atactgtgtg gtataacagg cttaataaat tctttaaaag 180  
 gaaaaaaa 188

<210> 301  
 <211> 291  
 <212> DNA  
 <213> Homo sapien

<400> 301  
 aagattttgt tttattttat tatggctaga aagacactgt tatagccaaa atcggcaatg 60  
 acactaaaga aatcctctgt gcttttcaat atgcaaatat atttcttcca agagttgccc 120  
 tgggtgtgact tcaagagttc atgttaactt cttttctgga aacttccttt tcttagttgt 180  
 tgtattcttg aagagccttg gccatgaaga gcttgccata gttttgggca gtgaactcct 240  
 tgatgttctg gcagtaagtg tttatctggc ctgcaatgag cagcgagtc a 291

<210> 302  
 <211> 341  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(341)  
 <223> n = A,T,C or G

<400> 302  
 tgatttttca taattttatt aaatnatcac tgggaaaact aatggttcgc gtatcacaca 60



```
attacactac aatctgatag gagtggtaaa accagccaat ggaatccagg taaagtacaa 120
aaacgccacc ttttattgtc ctgtcttatt tctcggaag gaggggtcta ctttacacat 180
ttcatgagcc agcagtggaac ttgagttaca atgtgtaggt tccttggtgt tatagctgca 240
gaagaagcca tcaaattctt gaggacttga catctctcgg aaagaagcaa actagtggat 300
ccccgggct gcaggaattc gatatcaagc ttatcgatac c 341
```

<210> 303

<211> 361

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (361)

<223> n = A,T,C or G

<400> 303

```
tgcagacagt aaatnaattt tatttgnngt cacagaacat actaggcgat ctcgacagtc 60
gctccgtgac agcccaccaa cccccaaccc tntacctgc agccacccta aaggcgactt 120
caanaanagt gaaggatctc acggatctca ttccaatgg tccgccgaag tctcacacag 180
tanacagacg gagttganat gctggaggat gcagtcacct cctaaactta cgaccaccca 240
ccanacttca tcccagccgg gacgtcctcc cccaccgag tcctcccat ttcttctct 300
actttgccgc agttccaggn gtctgcttc caccagtccc acaaagctca ataaatacca 360
a 361
```

<210> 304

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (301)

<223> n = A,T,C or G

<400> 304

```
ctctttacaa cagcctttat ttncggccct tgatcctgct cggatgctgg tggaggccct 60
tagctccgcc cgccaggctc tgtgccgcct ccccgaggc gcanattcat gaacacgggtg 120
ctcaggggct tgaggccgta ctccccagc gggagctggt cctccagggg ctccccctcg 180
aaggtcagcc anaacaggtc gtccctgcaca ccctccagcc cgctcacttg ctgcttcagg 240
tgggccacgg tctgcgtcag ccgcacctcg taggtgctgc tgcggccctt gttattctc 300
a 301
```

<210> 305

<211> 331

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (331)

<223> n = A,T,C or G

<400> 305

```
ganaggctag taacatcagt tttattgggt tggggnggca accatagcct ggctgggggn 60
```

ggggctggcc	ctcacaggtt	gttgagttcc	agcaggggtct	ggtccaaggt	ctggtgaatc	120
tcgaagttct	cctccttggc	actggccaag	gtctcttcta	ggtcacgat	ggttttctcc	180
aactttgcca	canacctctc	ggcaaaactct	gtcgggtct	cancctcctt	cagcttctcc	240
tccaacagtt	tgatctcctc	ttcataattta	tcttctttgg	gggaatactc	ctcctctgag	300
gccatcaggg	acttgagggc	ctggtccatg	g			331

&lt;210&gt; 306

&lt;211&gt; 457

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 306

aatatgtaaa	ggtaataact	tttattatat	taaagacaat	gcaaacgaaa	aacagaattg	60
agcagtgcaa	aatttaaagg	actgttttgt	tctcaaagtt	gcaagtttca	aagccaaaag	120
aattatatgt	atcaaata	taagtaaaaa	aaagtttagac	tttcaagcct	gtaatcccag	180
cactttggga	ggctgaggca	ggtggatcac	taacattaaa	aagacaacat	tagattttgt	240
cgatttatag	caattttata	aatatataac	tttgtcactt	ggatcctgaa	gcaaaaataat	300
aaagtgaatt	tgggattttt	gtacttggtg	aaaagtttaa	caccctaaat	tcacaactag	360
tggatccccc	gggtgcagg	aattcgatat	caagcttatc	gataccgtcg	acctcgaggg	420
ggggccccgt	acccaattcg	ccctatagtg	agtcgta			457

&lt;210&gt; 307

&lt;211&gt; 491

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 307

gtgcttgga	ggaacccggc	gtcgttccc	caccccgccc	ggccgccc	agccagccct	60
ccgtcacctc	ttcacccgac	cctcgactg	ccccaggcc	cccgcgcgcg	ctccagcgcc	120
ggcagccac	cgccgcgcgc	gcccctctc	cttagtcgc	gccatgacga	ccgcgtccac	180
ctcgagggtg	cgccagaact	accaccagga	ctcagaggcc	gccatcaacc	gccagatcaa	240
cctggagctc	tacgcctcct	acgtttacct	gtccatgtct	tactactttg	accgcgatga	300
tgtggctttg	aagaactttg	ccaaataactt	tcttcaccaa	tctcatgagg	agaggggaaca	360
tgctgagaaa	ctgatgaagc	tgcagaacca	acgaggtggc	cgaatcttcc	ttcaggatat	420
caagaaacca	gactgtgatg	actgggagag	cgggctgaat	gcaatggagt	gtgcattaca	480
tttggaaaaa	a					491

&lt;210&gt; 308

&lt;211&gt; 421

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 308

ctcagcgctt	cttctttctt	ggtttgatcc	tgactgctgt	catggcgtgc	cctctggaga	60
aggccctgga	tgtgatgggtg	tccaccttcc	acaagtactc	gggcaaagag	ggtgacaagt	120
tcaagctcaa	caagtcagaa	ctaaaggagc	tgctgacccg	ggagctgccc	agcttcttgg	180
ggaaaaggac	agatgaagct	gctttccaga	agctgatgag	caacttggac	agcaacaggg	240
acaacgaggt	ggacttccaa	gagtactgtg	tcttctgtc	ctgcatcgcc	atgatgtgta	300
acgaattctt	tgaaggcttc	ccagataaagc	agcccaggaa	gaaatgaaaa	ctcctctgat	360
gtgggtgggg	ggtctgccag	ctggggccct	ccctgtcgcc	agtgggcact	tttttttttc	420
c						421

&lt;210&gt; 309

&lt;211&gt; 321

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 309

accaa	atggc	ggatg	acgcc	ggtgc	agcgg	ggggg	ccccg	gggcc	ctggt	ggccct	ggga	60
tgggg	aaccg	cggtg	gcttc	cgcgg	aggtt	tcggc	agtgg	catcc	ggggc	cggggt	cgcg	120
gccgt	ggacg	gggcc	ggggc	cgagg	ccgcg	gagct	cgcgg	aggca	aggcc	gaggata	aagg	180
agtgg	atgcc	cgtca	ccaag	ttggg	ccgct	tggtc	aaagg	catga	agatc	aagtc	ccctgg	240
aggag	atcta	tctct	ttctc	ctgcc	atta	aggaat	caga	gatcat	tgat	ttcttc	ctgg	300
gggcct	ctct	caagg	atgag	g								321

&lt;210&gt; 310

&lt;211&gt; 381

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 310

ttaac	cagcc	atattg	gctc	aataa	atagc	ttcgg	taagg	agtta	atttc	cttct	tagaaa	60
tcagt	gccta	tttttc	ctgg	aaact	caatt	ttaaa	tagtc	caatt	ccatc	tgaag	ccaag	120
ctgtt	gtcat	tttcatt	ccg	tgacat	tctc	tcccat	gaca	cccaga	aagg	gcaga	agaac	180
cacatt	tttc	atttat	agat	gtttg	catcc	tttgt	attaa	aattat	tttg	aaggg	gttg	240
ctcatt	ggat	ggcttt	ttt	tttcct	cc	aggga	gaagg	ggaga	aatgt	acttg	gaaat	300
taatg	tatgt	ttacat	ctct	ttgca	aatc	ctgtac	atag	agata	tattt	tttaag	tgtg	360
aatgt	aacaa	catact	gtga	a								381

&lt;210&gt; 311

&lt;211&gt; 538

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 311

tttga	attta	cacca	agaac	ttctc	aataa	aagaaa	atca	tgaat	gctcc	acaatt	ttcaa	60
catacc	acaa	gagaag	ttaa	ttctt	aaca	ttgtg	ttcta	tgatt	atttg	taagac	cttc	120
accaag	ttct	gatat	ctttt	aaaga	catag	ttcaaa	attg	ctttt	gaaa	tctgt	attct	180
tgaaa	atata	cttgt	gtgt	attag	gtttt	taaat	accag	ctaaa	aggatt	acctc	actga	240
gtcat	cagta	ccctc	ctatt	cagct	cccc	agatg	atgtg	ttttt	gctta	cccta	agaga	300
ggttt	cttc	ttatt	tttag	ataatt	caag	tgctt	agata	aattat	gttt	tcttt	aaagt	360
tttat	ggtaa	actct	tttaa	agaaa	attta	atatg	ttata	gctga	atctt	tttggt	aaact	420
ttaaat	cttt	atcat	agact	ctgtac	atat	gttcaa	atta	gctg	cttgcc	tgatg	tgtgt	480
atcat	cggtg	ggatg	acaga	acaaac	atat	ttatg	atcat	gaata	atgtg	ctttgt	taa	538

&lt;210&gt; 312

&lt;211&gt; 176

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 312

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tcatag	aacc	attgc	cttag	aattat	tgtg	tgacac	gttt	tttgt	tggtt	aagct	gtaag	120
gtttt	gttct	ttgtg	aacat	gggtat	tttg	agggg	aggg	ggagg	gagta	gggaag		176

&lt;210&gt; 313

&lt;211&gt; 396

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 313

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gtcaccgggg	caactgcctg	ggggcgggga	tgggggcagg	gtggaagcgg	ctccccattt	360
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&lt;210&gt; 314

&lt;211&gt; 311

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 314

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&lt;210&gt; 315

&lt;211&gt; 336

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 315

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gttttgtaaa	cactatagca	tctgttaaga	tccagt			336

&lt;210&gt; 316

&lt;211&gt; 436

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 316

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atactttgaa	ccaaaagttg	cagagtgggtg	gaatgctatg	ttttaggaat	cagtccagat	360
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agggtctgta	taatca					436

&lt;210&gt; 317

&lt;211&gt; 196

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 317

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atgctccctc	ccctgccctg	gtccagggaa	gctggccgag	ggctctggct	cctgaggggc	180
atctgccct	ccccca					196

&lt;210&gt; 318

&lt;211&gt; 381

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (381)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 318

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tcttgaatcc	cancgatgaa	accannaact	cactttcccg	ggatgccgan	tctccattcc	300
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tccaagctcg	tggtggngg	a				381

&lt;210&gt; 319

&lt;211&gt; 506

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 319

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ttatacaggt	agagatgtat	gcagatgtgt	ccatatatgt	ccatatttac	atthttgatag	240
ccattgatgt	atgcatctct	tggtgttact	ataagaacac	attaattcaa	tggaatata	300
ccttgcta	atthttaat	tggtgttact	ataagaacac	attaattcaa	tggaatata	360
tctgttgctg	tggtgttcat	tttaaatga	gcattaagg	aatgcagcat	ttaaatcaga	420
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&lt;210&gt; 320

&lt;211&gt; 351

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 320

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tccaagagag	gatccgagaa	cgctctaagc	ctgtccacga	gctcaatagg	gaagcctgtg	240
atgactacag	actttgca	cgctacgcca	tggtttatgg	atacaatgct	gcctataatc	300
gctacttcag	gaagcgccga	gggaccaa	gagactgagg	gaagaaaaa	a	351

&lt;210&gt; 321

<211> 421  
 <212> DNA  
 <213> Homo sapien

<400> 321  
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 c 421

<210> 322  
 <211> 521  
 <212> DNA  
 <213> Homo sapien

<400> 322  
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 gtgctgaaac gaccggagat actgacagat gagagcctca gcagcttggc agtctcatgt 180  
 ccccttacct cacttgtctc tagccgcagc ttccaaacca gcgccatttc aagggaacac 240  
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 ttttgtctga tggtagcctt tctcatcctc tttgccatgt gaaggagccg tctccacctc 480  
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<210> 323  
 <211> 435  
 <212> DNA  
 <213> Homo sapien

<400> 323  
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 atcttggaaca gcgtgggtat cgaggcggac gacgaccggc tcaacaaggt tatcagtga 180  
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 gatgatgaca tgggatttgg cctttttgat taaattcctg ctcccctgca aataaagcct 420  
 ttttacacat ctcaa 435

<210> 324  
 <211> 521  
 <212> DNA  
 <213> Homo sapien

<400> 324  
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 aaccccgacc tcagcctcag ccgcaacccc agccccaatc acaaccccag cctcagcccc 240

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cacacccaca	gccgcactcg	cagccgcacg	ggcaccggct	tctccgcagc	acctccaact	420
ctgcctgaaa	ggggcagctc	ccgggcaaga	caaggttttg	aggacttgag	gaagtgggac	480
gagcacattt	ctattgtctt	cacttggatc	aaaagcaaaa	c		521

&lt;210&gt; 325

&lt;211&gt; 451

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 325

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ctttatcact	tgaattatta	acttaatttg	a			451

&lt;210&gt; 326

&lt;211&gt; 421

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (421)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 326

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tcacaagcga	ctcattgact	tgcacagtcc	ttctgagatt	gttaagcaga	ttacttccat	420
c						421

&lt;210&gt; 327

&lt;211&gt; 456

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 327

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<210> 328  
 <211> 471  
 <212> DNA  
 <213> Homo sapien

<400> 328  
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<210> 329  
 <211> 278  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(278)  
 <223> n = A,T,C or G

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 <211> 338  
 <212> DNA  
 <213> Homo sapien

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<210> 331  
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 <212> DNA  
 <213> Homo sapiens

<400> 331  
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&lt;210&gt; 332

&lt;211&gt; 2270

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 332

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 333

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&lt;211&gt; 2082

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 334

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&lt;211&gt; 4849

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 335

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cctcagggag ctgttatccg cgccatgcct gtctacaaaa aagctgagca cgtcacggag 600
gtggtgaagc ggtgccccaa ccatgagctg agccgtgaat tcaacgaggg acagattgcc 660
cctcctagtc atttgattcg agtagagggg aacagccatg cccagtatgt agaagatccc 720

```

```

atcacaggaa gacagagtgt gctggtacct tatgagccac cccaggttgg cactgaattc 780
acgacagtct tgtacaattt catgtgtaac agcagttgtg ttggagggat gaaccgccgt 840
ccaattttta tcatgtttac tctggaaacc agagatgggc aagtcctggg ccgacgctgc 900
tttgaggccc ggatctgtgc ttgcccagga agagacagga aggcggatga agatagcatc 960
agaaagcagc aagtttcgga cagtacaaag aacggtgatg gtacgaagcg cccgtttcgt 1020
cagaacacac atggtatcca gatgacatcc atcaagaaac gaagatcccc agatgatgaa 1080
ctgttatact taccagttag gggccgtgag acttatgaaa tgctgttgaa gatcaaagag 1140
tccctggaac tcatgcagta ccttcctcag cacacaattg aaacgtacag gcaacagcaa 1200
cagcagcagc accagcactt acttcagaaa cagacctcaa tacagtctcc atcttcatat 1260
ggtaacagct cccacactct gaacaaaatg aacagcatga acaagctgcc ttctgtgagc 1320
cagcttatca accctcagca gcgcaacgcc ctactccta caaccattcc tgatggcatg 1380
ggagccaaca ttcccatgat gggcaccac atgccaatgg ctggagacat gaatggactc 1440
agccccaccc aggcactccc tccccactc tccatgccat ccacctcca ctgcacaccc 1500
ccacctcctg atcccacaga ttgcagcatt gtcaggatct ggcaagtctg a 1551

```

&lt;210&gt; 338

&lt;211&gt; 586

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 338

```

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
          5                      10                      15

```

```

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Arg Asn
          20                      25                      30

```

```

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
          35                      40                      45

```

```

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Pro Thr Phe Asp Ala
          50                      55                      60

```

```

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
          65                      70                      75                      80

```

```

His Ser Ser Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
          85                      90                      95

```

```

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
          100                      105                      110

```

```

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
          115                      120                      125

```

```

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
          130                      135                      140

```

```

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
          145                      150                      155                      160

```

```

Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
          165                      170                      175

```

```

Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val

```

180	185	190
Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val		
195	200	205
Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg		
210	215	220
Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val		
225	230	235
Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg		
245	250	255
Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp		
260	265	270
Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr		
275	280	285
His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp		
290	295	300
Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu		
305	310	315
Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His		
325	330	335
Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu		
340	345	350
Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser		
355	360	365
Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val		
370	375	380
Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr		
385	390	395
Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met		
405	410	415
Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro		
420	425	430
Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro		
435	440	445
Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys		
450	455	460
Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr		
465	470	475
		480



Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro  
485 490 495

Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln  
500 505 510

Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser  
515 520 525

Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val  
530 535 540

Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro  
545 550 555 560

Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn  
565 570 575

Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu  
580 585

<210> 339

<211> 641

<212> PRT

<213> Homo sapiens

<400> 339

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe  
5 10 15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro  
20 25 30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn  
35 40 45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu  
50 55 60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
65 70 75 80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
85 90 95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
100 105 110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
115 120 125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
130 135 140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335  
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
 355 360 365  
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu  
 370 375 380  
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400  
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser  
 405 410 415  
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser  
 420 425 430  
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg

435                      440                      445  
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile  
 450                      455                      460  
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu  
 465                      470                      475                      480  
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser  
 485                      490                      495  
 His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly  
 500                      505                      510  
 Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr  
 515                      520                      525  
 Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp  
 530                      535                      540  
 Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys  
 545                      550                      555                      560  
 Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His  
 565                      570                      575  
 Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser  
 580                      585                      590  
 Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg  
 595                      600                      605  
 Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe  
 610                      615                      620  
 Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly  
 625                      630                      635                      640

Glu

<210> 340  
 <211> 448  
 <212> PRT  
 <213> Homo sapiens

<400> 340  
 Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe  
                     5                      10                      15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro  
                     20                      25                      30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn  
                     35                      40                      45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu  
 50 55 60  
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
 65 70 75 80  
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
 85 90 95  
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
 100 105 110  
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
 115 120 125  
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
 130 135 140  
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335

Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350

Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
 355 360 365

Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu  
 370 375 380

Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400

Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys  
 405 410 415

Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser  
 420 425 430

Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro  
 435 440 445

<210> 341

<211> 356

<212> PRT

<213> Homo sapiens

<400> 341

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
 5 10 15

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
 20 25 30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
 35 40 45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
 50 55 60

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65 70 75 80

His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
 85 90 95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
 100 105 110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
 115 120 125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
 130 135 140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn

145                      150                      155                      160  
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn  
                                  165                      170                      175  
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
                                  180                      185                      190  
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
                                  195                      200                      205  
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
                                  210                      215                      220  
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
                                  225                      230                      235                      240  
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg  
                                  245                      250                      255  
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
                                  260                      265                      270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Ser Arg Gln Asn Thr  
                                  275                      280                      285  
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
                                  290                      295                      300  
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
                                  305                      310                      315                      320  
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
                                  325                      330                      335  
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu  
                                  340                      345                      350  
 Leu Gln Lys Gln  
                                  355  
 <210> 342  
 <211> 680  
 <212> PRT  
 <213> Homo sapiens  
 <400> 342  
 Met Asn Phe Glu Thr Ser Arg Cys Ala Thr Leu Gln Tyr Cys Pro Asp  
                                  5                      10                      15  
 Pro Tyr Ile Gln Arg Phe Val Glu Thr Pro Ala His Phe Ser Trp Lys  
                                  20                      25                      30  
 Glu Ser Tyr Tyr Arg Ser Thr Met Ser Gln Ser Thr Gln Thr Asn Glu  
                                  35                      40                      45

Phe Leu Ser Pro Glu Val Phe Gln His Ile Trp Asp Phe Leu Glu Gln  
 50 55 60  
 Pro Ile Cys Ser Val Gln Pro Ile Asp Leu Asn Phe Val Asp Glu Pro  
 65 70 75 80  
 Ser Glu Asp Gly Ala Thr Asn Lys Ile Glu Ile Ser Met Asp Cys Ile  
 85 90 95  
 Arg Met Gln Asp Ser Asp Leu Ser Asp Pro Met Trp Pro Gln Tyr Thr  
 100 105 110  
 Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn Gly Ser  
 115 120 125  
 Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser Val Thr  
 130 135 140  
 Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala Leu Ser  
 145 150 155 160  
 Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His Ser  
 165 170 175  
 Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp  
 180 185 190  
 Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr  
 195 200 205  
 Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly Ala Val  
 210 215 220  
 Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr Glu Val  
 225 230 235 240  
 Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn Glu Gly  
 245 250 255  
 Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn Ser His  
 260 265 270  
 Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val Leu Val  
 275 280 285  
 Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val Leu Tyr  
 290 295 300  
 Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg Arg Pro  
 305 310 315 320  
 Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val Leu Gly  
 325 330 335

Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg  
 340 345 350  
 Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp Ser Thr  
 355 360 365  
 Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr His Gly  
 370 375 380  
 Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp Glu Leu  
 385 390 395 400  
 Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu Leu Lys  
 405 410 415  
 Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His Thr Ile  
 420 425 430  
 Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu Leu Gln  
 435 440 445  
 Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser Ser Pro  
 450 455 460  
 Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val Ser Gln  
 465 470 475 480  
 Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr Ile Pro  
 485 490 495  
 Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met Pro Met  
 500 505 510  
 Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro Pro Pro  
 515 520 525  
 Leu Ser Met Pro Ser Thr Ser Gln Cys Thr Pro Pro Pro Pro Tyr Pro  
 530 535 540  
 Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys Ser Ser  
 545 550 555 560  
 Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr Gln Ile  
 565 570 575  
 Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro Glu Gln  
 580 585 590  
 Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln Leu His  
 595 600 605  
 Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser Ala Ser  
 610 615 620  
 Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val Ile Asp



625                      630                      635                      640  
 Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro Arg Asp  
                          645                      650                      655  
 Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn Lys Gln  
                          660                      665                      670  
 Gln Arg Ile Lys Glu Glu Gly Glu  
                          675                      680

<210> 343  
 <211> 461  
 <212> PRT  
 <213> Homo sapiens

<400> 343  
 Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
                          5                      10                      15  
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
                          20                      25                      30  
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
                          35                      40                      45  
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
                          50                      55                      60  
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
                          65                      70                      75                      80  
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
                          85                      90                      95  
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
                          100                      105                      110  
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
                          115                      120                      125  
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
                          130                      135                      140  
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
                          145                      150                      155                      160  
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn  
                          165                      170                      175  
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
                          180                      185                      190  
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
                          195                      200                      205

Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
 210 215 220  
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
 225 230 235 240  
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg  
 245 250 255  
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
 260 265 270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
 275 280 285  
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
 290 295 300  
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
 325 330 335  
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu  
 340 345 350  
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser  
 355 360 365  
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
 370 375 380  
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
 385 390 395 400  
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met  
 405 410 415  
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro  
 420 425 430  
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro  
 435 440 445  
 Tyr Pro Thr Asp Cys Ser Ile Val Arg Ile Trp Gln Val  
 450 455 460

&lt;210&gt; 344

&lt;211&gt; 516

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 344



```

290                295                300
Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
305                310                315                320
Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
325                330                335
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
340                345                350
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
355                360                365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
370                375                380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
385                390                395                400
Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser
405                410                415
Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser
420                425                430
Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg
435                440                445
Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
450                455                460
Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
465                470                475                480
Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
485                490                495
His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Arg
500                505                510
Ile Trp Gln Val
515

```

&lt;210&gt; 345

&lt;211&gt; 1800

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 345

```

gcgccctcatt gccactgcag tgactaaagc tggaagacg ctggtcagtt cacctgcccc 60
actggttggt ttttaaaca attctgatac aggcgacatc ctactgacc gagcaaagat 120
tgacattcgt atcatcactg tgcaccattg gcttctaggc actccagtgg ggtaggagaa 180

```

```

ggaggtctga aaccctcgca gagggatctt gccctcattc tttgggtctg aaacactggc 240
agtcgttgga aacaggactc agggataaac cagcgcaatg gattggggga cgctgcacac 300
tttcatcggg ggtgtcaaca aacactccac cagcatcggg aaggtgtgga tcacagtcac 360
ctttattttc cgagtcacga tcttagtggt ggctgcccag gaagtgtggg gtgacgagca 420
agaggacttc gtctgcaaca cactgcaacc gggatgcaaa aatgtgtgct atgaccactt 480
tttcccggtg tcccacatcc ggctgtgggc cctccagctg atcttcgtct ccaccccagc 540
gctgctggtg gccatgcatg tggcctacta caggcacgaa accactcgca agttcaggcg 600
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atgtgggatt gacccctgcc ccaaccttgt tgactgcttt atttctaggg caacagagaa 840
gaccgtgttt accattttta tgatttctgc gtctgtgatt tgcacgtgc ttaacgtggc 900
agagttgtgc tacctgctgc tgaaagtgtg ttttaggaga tcaaagagag cacagacgca 960
aaaaaatcac cccaatcatg ccctaaagga gagtaagcag aatgaaatga atgagctgat 1020
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acggaacagt gtggaagcag aaggcttttt taactcatcc gtttggccga tcgttgacga 1740
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&lt;210&gt; 346

&lt;211&gt; 261

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 346

```

Met Asp Trp Gly Thr Leu His Thr Phe Ile Gly Gly Val Asn Lys His
          5              10              15

```

```

Ser Thr Ser Ile Gly Lys Val Trp Ile Thr Val Ile Phe Ile Phe Arg
          20              25              30

```

```

Val Met Ile Leu Val Val Ala Ala Gln Glu Val Trp Gly Asp Glu Gln
          35              40              45

```

```

Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
          50              55              60

```

```

Tyr Asp His Phe Phe Pro Val Ser His Ile Arg Leu Trp Ala Leu Gln
          65              70              75              80

```

```

Leu Ile Phe Val Ser Thr Pro Ala Leu Leu Val Ala Met His Val Ala
          85              90              95

```

```

Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
          100              105              110

```

Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys His Lys Val Arg Ile  
 115 120 125  
 Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Ile  
 130 135 140  
 Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly  
 145 150 155 160  
 Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn  
 165 170 175  
 Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr  
 180 185 190  
 Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala  
 195 200 205  
 Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg  
 210 215 220  
 Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys  
 225 230 235 240  
 Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile  
 245 250 255  
 Thr Gly Phe Pro Ser  
 260

&lt;210&gt; 347

&lt;211&gt; 1740

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 347

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 ttcgtggact gcccgacga gagctgggccc ctcaaggcca tcgaggcgct ttcaggtaaa 180  
 atagaactgc acgggaaacc catagaagtt gagcactcgg tcccaaaaag gcaaaggatt 240  
 cggaaacttc agatacgaaa tatccgcct catttacagt gggaggtgct ggatagttaa 300  
 ctagtccagt atggagtggg ggagagctgt gagcaagtga aactgactc ggaaactgca 360  
 gttgtaaagt taacctattc cagtaaggac caagctagac aagcactaga caaactgaat 420  
 ggatttcagt tagagaattt caccttgaaa gtagcctata tccctgatga aacggccgccc 480  
 cagcaaaacc ccttgcagca gccccgaggt cgccgggggc ttgggcagag gggctcctca 540  
 aggcaggggg ctcaggatc cgtatccaag cagaaaacat gtgatttgcc tctgcgcctg 600  
 ctgggttccca cccaatttgt tggagccatc ataggaaaag aaggtgccac cattcggaac 660  
 atcaccaaac agaccagtc taaaatcgat gtccaccgta aagaaaatgc gggggctgct 720  
 gagaagtcga ttactatcct ctctactcct gaaggcacct ctgcggttg taagtctatt 780  
 ctggagatta tgcataagga agctcaagat ataaaattca cagaagagat ccccttgaag 840  
 attttagctc ataataactt tgttggacgt cttattggta aagaaggaag aaatcttaaa 900  
 aaaattgagc aagacacaga cactaaaatc acgatatctc cattgcagga attgacgctg 960

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<210> 348
<211> 579
<212> PRT
<213> Homo sapiens
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Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Glu Asn Ala Ala Pro Ser  
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Asp Leu Glu Ser Ile Phe Lys Asp Ala Lys Ile Pro Val Ser Gly Pro  
20 25 30

Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser  
35 40 45

Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His  
50 55 60

Gly Lys Pro Ile Glu Val Glu His Ser Val Pro Lys Arg Gln Arg Ile  
65 70 75 80

Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val  
85 90 95

Leu Asp Ser Leu Leu Val Gln Tyr Gly Val Val Glu Ser Cys Glu Gln  
100 105 110

Val	Asn	Thr	Asp	Ser	Glu	Thr	Ala	Val	Val	Asn	Val	Thr	Tyr	Ser	Ser
	115						120					125			

Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu  
130 135 140

Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Thr Ala Ala  
145 150 155 160

Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly Gln  
165 170 175

Arg Gly Ser Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys

180	185	190
Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln Phe Val Gly		
195	200	205
Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln		
210	215	220
Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala		
225	230	235 240
Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala		
245	250	255
Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys		
260	265	270
Phe Thr Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Asn Phe Val		
275	280	285
Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln		
290	295	300
Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu		
305	310	315 320
Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys		
325	330	335
Ala Lys Ala Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu		
340	345	350
Asn Asp Ile Ala Ser Met Asn Leu Gln Ala His Leu Ile Pro Gly Leu		
355	360	365
Asn Leu Asn Ala Leu Gly Leu Phe Pro Pro Thr Ser Gly Met Pro Pro		
370	375	380
Pro Thr Ser Gly Pro Pro Ser Ala Met Thr Pro Pro Tyr Pro Gln Phe		
385	390	395 400
Glu Gln Ser Glu Thr Glu Thr Val His Leu Phe Ile Pro Ala Leu Ser		
405	410	415
Val Gly Ala Ile Ile Gly Lys Gln Gly Gln His Ile Lys Gln Leu Ser		
420	425	430
Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp		
435	440	445
Ala Lys Val Arg Met Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe		
450	455	460
Lys Ala Gln Gly Arg Ile Tyr Gly Lys Ile Lys Glu Glu Asn Phe Val		
465	470	475 480



Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser  
485 490 495

Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu  
500 505 510

Leu Gln Asn Leu Ser Ser Ala Glu Val Val Val Pro Arg Asp Gln Thr  
515 520 525

Pro Asp Glu Asn Asp Gln Val Val Val Lys Ile Thr Gly His Phe Tyr  
530 535 540

Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val  
545 550 555 560

Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser  
565 570 575

Arg Arg Lys

<210> 349

<211> 207

<212> DNA

<213> Homo sapiens

<400> 349

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gaaaagatga gagaagttac agactctcct gggcgacccc gagagcttac cattctcag 180  
acttcttcac atgggtgctaa cagattt 207

<210> 350

<211> 69

<212> PRT

<213> Homo sapiens

<400> 350

Met Trp Gln Pro Leu Phe Phe Lys Trp Leu Leu Ser Cys Cys Pro Gly  
5 10 15

Ser Ser Gln Ile Ala Ala Ala Ala Ser Thr Gln Pro Glu Asp Asp Ile  
20 25 30

Asn Thr Gln Arg Lys Lys Ser Gln Glu Lys Met Arg Glu Val Thr Asp  
35 40 45

Ser Pro Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr Ser Ser His  
50 55 60

Gly Ala Asn Arg Phe  
65

